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REPORT OF AN OUTBREAK OF FEBRILE ILLNESS WITH PHARYNGEAL LESIONS AND EXANTHEM: TORONTO, SUMMER 1957 — ISOLATION OF GROUP A COXSACKIE VIRUS*

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DURING the last ten years, the use of suckling mice and of tissue cultures has led to the isolation of large numbers of hitherto undescribed viruses, many of which have now been identified as the cause of human disease.[52] The spectrum of clinical manifestation of infection caused by several of these viruses is wide, and many clinical syndromes of previously unknown etiology have now been shown to be examples of infection with these newly discovered agents. On the other hand, the pathogenic role of some of these "new" viruses has not yet been established, and it has become increasingly evident that certain rigid criteria must be fulfilled before the causal role of such viruses in human infection may be regarded as proven.[23, 48]

The newer viruses include the Coxsackie and Echo viruses, members of the group of "enteric" viruses. The Coxsackie viruses were first isolated by Dalldorf and Sickles in 1947, and comprise two distinct biological groups, A and B. Several types of Group A virus cause herpangina. The role of Group A Coxsackie virus in the causation of aseptic meningitis and of short-term fevers is less well established. Group B viruses cause epidemic myalgia (Bornholm disease), aseptic meningitis and infantile myocarditis. The full range of pathogenicity of the Coxsackie viruses has yet to be determined.[43, 51]

During the end of June and the early part of July 1957, an outbreak of a short-term febrile illness with some unusual features occurred in a suburb of Toronto.[18] The characteristic feature of the illness was the presence of a maculopapular or vesicular exanthem associated with pharyngeal lesions. The illness was mild and admission to hospital was not necessary. All cases were referred to us by private physicians and were seen in the home by one of us (C.R.R.) as part of a project undertaken by the School of Hygiene, University of Toronto, in the investigation of epidemics of virus diseases by combined field and laboratory work. Laboratory studies revealed the presence in pathological specimens from most cases of this illness of a virus pathogenic both for tissue cultures and for suckling mice, and having the general characters of a member of the Coxsackie family, Group A. At the New York State Laboratories in Albany, N.Y., the Toronto strain was found to be immunologically related to Coxsackie type A16, a serotype first isolated by Gear in South Africa.[16, 17, 49, 50] Our own laboratory results confirm such a relationship.

It is the purpose of this paper to provide a full account of the clinical and epidemiological features of this illness, and to give a preliminary account of virus studies still in progress.

CLINICAL FEATURES

Over a period of about four weeks in June and July 1957, 60 persons affected by the illness were investigated. The onset of illness occurred with fever, malaise and a sore throat or mouth. The illness was mild and most patients recovered after a week. The clinical features are summarized in Table I. The following observations may be made.

1. *Fever.*—A history of fever was reported in over half the patients (56.6%). The fever lasted two or three days and temperatures on an average reached 101° F.; in four patients the temperature exceeded 104° F.

2. *Oral and faucial lesions.*—A history of sore throat or mouth was obtained from 31 patients (51.6%). On examination, a larger number (76.5%) showed lesions of the oropharynx or fauces. The lesions consisted of a simple redness or of ulcers on an inflammatory background. The ulcers were preceded by vesicles which had in turn developed from small red macules. The vesicles were oval and

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TABLE I.—GROUP A COXSACKIE INFECTION WITH EXANTHEM AND PHARYNGEAL LESIONS: THE FREQUENCY OF CLINICAL FEATURES IN 60 PATIENTS

Symptoms	
Fever	34 (56.6%)
Sore throat or mouth	31 (51.6%)
Malaise	29 (48.3%)
Anorexia	13 (21.1%)
Abdominal pain	7 (11.6%)
Diarrhœa	5 (8.3%)
Nausea	2 (3.3%)
Vomiting	2 (3.3%)
Cough	11 (18.3%)
Coryza	8 (13.3%)
Chest pain	1 (1.6%)
Headache	6 (10.0%)
Signs	
Throat or oropharyngeal lesion	46 (76.5%)
Maculopapular rash	24 (40.0%)
Vesicular rash	15 (25.0%)
Conjunctival injection	11 (18.3%)
Exanthem	1 (1.6%)

varied in size from 1 to 3 mm. in diameter. Some of these vesicles ulcerated, while the contents of others were absorbed uneventfully. It was often possible to see ulcers and vesicles side by side. The larger ulcers arose from a coalescence of smaller vesicles, and the bullous lesion so formed usually broke down. In one patient, a painful bulla occurred on the side of the tongue, but the contents were absorbed in the course of a few days.

The oral ulcers varied from 1 to 2 cm. across and were shallow with a yellowish-grey base and a hyperæmic margin. They occurred on the tongue, on the inside of the cheeks, in the gingivo-labial groove, and on the hard palate or uvula. Such lesions of the oropharynx were found in 22 cases.

The lesions in the fauces appeared as a simple redness in 14 cases. In an additional 16 patients, there were ulcers similar to but smaller than those seen in the mouth.

3. *Exanthem.*—A skin rash was present in 24 cases. The rash was maculopapular in all patients. In 15 of these cases there was in addition a vesicular rash. The vesicles developed from macules and these thin-walled blisters were superficial in the skin and non-loculated and contained clear watery fluid. Vesicles varied in size from 0.5 to 1 cm. in diameter, and were oval or circular with a narrow zone of erythema surrounding the base of the lesion. The eruption was not profuse, and only two or three vesicles might be present at any one time.

TABLE II.—GROUP A COXSACKIE INFECTION WITH EXANTHEM AND PHARYNGEAL LESIONS: DISTRIBUTION OF EXANTHEM IN 24 PATIENTS

Site of rash	*Number of patients with rash* Maculopapular	Vesicular
Hands	12	10
Feet	11	10
Upper limbs	10	2
Lower limbs	9	2
Chest	4	0
Abdomen	4	0
Face	2	2
Genitalia	0	1

The vesicles caused little discomfort, were not itchy and absorbed in the course of three to four days, leaving a small red spot. The distribution of the exanthem was centrifugal (Table II), and the limbs, hands and feet were most often affected. The vesicles occurred most commonly on the dorsum of the fingers and toes and on the lateral border of the feet. They were not often seen on the palms and soles, but when they did occur they were more profuse than elsewhere, were deep-seated, and resembled small grains of rice. In one child, 16 months of age, a vesicular rash was present at the base of the penis.

4. *Respiratory symptoms.*—Cough, coryza or chest pain was reported in a total of 20 patients (33.3%).

5. *Gastro-intestinal symptoms.*—These symptoms occurred in 20 patients (33.3%) and comprised marked anorexia, nausea, vomiting, abdominal pain, and diarrhœa.

6. *Conjunctival injection.*—This occurred in 11 patients (18.3%), and in two was the most marked feature of the illness.

7. *Other features.*—Complaint of a frontal or generalized headache was made by six patients (10%), all of whom were adults.

White cell counts performed on a few patients in the acute phase of the illness showed a normal total count; the differential count showed a relative lymphocytosis and monocytosis, and many of the mononuclears were atypical. Paul-Bunnell agglutination tests performed at appropriate times during the course of the illness in three patients were negative.

A follow-up investigation of 12 patients four months after the onset of illness confirmed the absence of sequelæ. It is of some interest that four babies, born at the end of 1957 to mothers who had resided in the housing estate during the outbreak of illness, were found to have mild congenital abnormalities. One had a Klippel-Feil syndrome, one an imperforate anus, one a dermal sinus of the neck, and another a cleft palate. There is no definite history that the mothers had been affected by this illness.

EPIDEMIOLOGY

The housing estate in which the outbreak arose extends over an area of 2300 acres and lies ten miles northeast of the centre of Toronto. It is divided by two main roads into four quadrants of an approximately equal size. The illness started in the south-east quadrant, spread to the south-west and north-west quadrants, and some weeks later appeared in the north-east.

The distribution of cases in relation to the topography of the estate is shown in Fig. 1. From this figure it can be seen that 34 cases occurred in the south-west quadrant (56%), 15 cases in the south-

Fig. 1.—Group A Coxsackie virus infection with vesicular exanthem and pharyngeal lesions. The distribution of cases in relation to the topography of the housing estate.

east (25%), seven cases in the north-west (11.7%) and four cases in the north-east quadrant (6.6%).

Most patients with an exanthem lived in the south-west quadrant, and similarly, all but one of those who showed vesiculation were from this area. A further two patients from the north-west quadrant and one from the north-east quadrant had rashes.

A total of 27 families was affected. The age distribution was as follows:

Children (mean age 3.4 years)	
0- 6 months	4
7-11 months	1
1- 4 years	29
5- 9 years	13
Total	47
Adults (mean age 31 years)	13

The incubation period of the illness was short, about three to five days. In one case, a child was taken ill with a vesicular rash five days after his family had moved into the housing estate from a distant part. Similarly, an adult became sick five days after exposure to infection.

The illness was highly infectious, for as can be seen from Table III, clinical illness developed in 60 of the 115 members of the affected households (52%). The illness spread progressively through adjacent block of houses, and also from one family to another.

The composition of the population under study by year of age, and the incidence of primary and secondary cases in the affected age groups, are shown in Table III. It can be seen from this table that the majority of cases of illness occurred in the 50 members of the one to nine year age group. There the number of cases of primary infection (30) was far in excess of the secondary cases (12). These facts suggested that the children were infected outside the home and that there was a common mode of infection for this age group. Amongst adults, and below the age of 12 months, this distribution did not apply. The temporal distribution of cases also suggested that adults and infants were infected in the home, infection being introduced by children of the one to nine year age group.

TABLE III.—GROUP A COXSACKIE INFECTION WITH EXANTHEM AND PHARYNGEAL LESIONS: COMPOSITION OF THE POPULATION UNDER STUDY BY YEAR OF AGE, AND INCIDENCE OF PRIMARY AND SECONDARY CASES IN THE AFFECTED AGE GROUPS

Age	*Total population of affected households*	*Clinical illness*		
		*Primary cases**	*Secondary cases*	*Total*
0-11 months	9	0	5	5
1- 4 years	32	19	10	29
5- 9 years	18	11	2	13
Adults	56	3	10	13
Total	115	33	27	60

*Primary cases were considered to be those which occurred first in the household and also those cases occurring within 24 hours of the onset of the first case.

A factor of probable importance in the spread of infection was the nature of the back gardens of the individual groups of houses. There were no fences, hedges, or other barriers between the gardens, and the children being on vacation played in the gardens of neighbouring houses as if the area constituted a communal playground. The weather, as usual for the time of year, was hot and humid, and most families owned small portable swimming pools used by their own and neighbouring children. The close contact of the children at play, particularly in these communal swimming pools, may help to explain the high incidence of primary infection in the one to nine year age group.

VIRUS STUDIES

Isolations.—Throat swabs and specimens of stool and blood were obtained at the first visit to each patient. A further sample of blood was collected four weeks later, when possible. Stools were prepared by ultracentrifugation, the deposit being resuspended in tissue culture medium to which 250 units of penicillin and 100 micrograms of streptomycin were added per ml.

Attempts at virus isolation were made by the inoculation of specimens from 31 patients (Table IV). Virus was isolated from 22 of these patients (71%). Of the specimens tested, 17 were throat swabs, 27 were stools, 2 were blood in the acute phase (obtained during the first 48 hours after onset of illness), and one specimen consisted of the clear fluid from a skin vesicle.

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TABLE IV.—GROUP A COXSACKIE INFECTION WITH EXANTHEM AND PHARYNGEAL LESIONS: VIRUS ISOLATION TESTS ON 31 PATIENTS

	Isolations of virus made by following techniques		
Specimens	*Tissue culture**	*Suckling mice*	*Total isolation*
Stool	18/27 (67%)	16/20 (80%)	22/27 (79%)
Throat	2/13 (15%)	3/13 (23%)	4/17 (23%)
Acute phase blood	0/2		0/2
Vesicle fluid	0/1	0/1	0/1
Total patients	18/30 (60%)	16/29 (55%)	22/31 (71%)

*The tissue cultures used were monolayer monkey kidney epithelial cell cultures.

From the 27 stool preparations, 22 virus strains were isolated, but from the 17 throat swabs only 4 strains were recovered. Attempts to isolate the virus from the two specimens of blood and the vesicle fluid were not successful. The viruses were ether resistant, and cytopathogenic in monolayer tissue cultures, and produced myositis in suckling mice inoculated directly with stool suspension or throat washings, as described below.

Tissue culture tests.—Growth of the virus occurred with the production of cytopathogenic changes in monkey kidney and human amnion tissue cultures. Intracytoplasmic "inclusions" typical of the enteric virus group were demonstrated. After several passages of the strain, cytopathogenic changes in monkey kidney cells occurred in 24-48 hours. Human amnion cells were not as susceptible as monkey kidney cells, growth of virus was slow and poor, and often no cytopathogenic changes appeared for 7-15 days. Furthermore, this system was a less sensitive indicator of the presence of virus in the specimens tested.

These cytopathogenic agents were tested for neutralization by available antisera to the cytopathogenic enteric viruses. None of 18 strains was neutralized by monotypic antiserum to the following viruses: poliomyelitis types 1, 2, and 3; Coxsackie virus Group A, type 9; Coxsackie virus Group B, types 1-5; Echo virus types 1-12 and type 14.

As it was soon found that the strains were pathogenic for suckling mice, producing myositis, infected tissue culture material was submitted to the New York State Laboratories, Albany, for further study. They reported that in suckling mice the Toronto virus was not neutralized by antisera to additional members of the Coxsackie A family with the exception of Coxsackie virus Group A, type 16.

The prototype Coxsackie A16 strain, in the form of infected suckling mouse tissue, was kindly sent to us. We found that this virus was cytopathogenic in monkey kidney cultures. A16 virus was used in virus neutralization tests run in tissue culture with acute and convalescent phase serum from four patients. As seen in Table V, a significant rise in neutralizing antibody to type A16 was demonstrated in two patients, and the results in a third (C.M.) were also consistent with current infection. Additional evidence bearing on the relationship between the Toronto strain and the prototype A16 strain is afforded by the demonstration that antiserum to one strain of the Toronto virus, prepared in hamsters, neutralized prototype A16 virus to a titre of 1:64. A finding, as yet unexplained, was the low titre of this hamster serum to the homologous virus (approximately 1:10).

Mouse pathogenicity.—As shown in Table IV, pathological specimens from 29 patients were inoculated intraperitoneally and intracerebrally into day-old suckling mice; specimens from 16 of the patients produced myositis on direct inoculation in suckling mice (55%).

A comparison was made of the mouse pathogenicity of the prototype A16 virus with the currently isolated Toronto strains. The manifestations of illness and the histological changes produced in the mice by each agent appeared identical, and were typical of those customarily found in Group A Coxsackie virus infection. Early paralysis of the hind limbs, with later paralysis of the front limbs, was a common finding. On primary isolation, several strains produced only patchy myositis which was most noticeable in the intercostal muscles. Subsequent passage of these strains caused generalized severe myositis typical of Group A Coxsackie infection. The incubation period in early transfers was about five days, but dropped to three days when the strains were adapted.

Although the characteristics of the viruses isolated were not those of herpes simplex virus, additional tests for this agent were made. Specimens from throat swabs from seven patients who showed oral lesions were inoculated on to rabbit corneas, into guinea-pig foot pads, and adult mice. All these tests proved negative. Neutralization tests performed with a Toronto strain of herpes virus known as H51[11] failed to demonstrate neutralizing antibodies in either acute or convalescent phase specimens of two patients (Table V). Scrapings

TABLE V.—GROUP A COXSACKIE INFECTION WITH EXANTHEM AND PHARYNGEAL LESIONS: RESULTS OF VIRUS NEUTRALIZATION TESTS

Patient	*Age (years)*	*Serum specimen collected on day after onset*	*Neutralization titres of sera in tests with following viruses**	
			Coxsackie A16 (prototype)	*Herpes simplex*
C.B.	2	7	1:5	1:8
		25	1:125	1:8
		179	1:25	
P.B.	32	2	1:5	
		20	1:5	
		153	1:5	
C.M.	7	14	1:32	1:8
		30	1:64	1:8
A.L.	3½	7	1:32	
		171	1:128	

*Test dose of virus used = 50 TCD_{50}.

of the base of the vesicular skin lesions did not show Tzank cells. Similar smears stained by Giemsa showed no rickettsiæ or bacteria.

DISCUSSION

One of the most significant findings in the laboratory investigation was the recovery of a virus from 22 of the 31 patients tested (71%). This virus has the characteristic properties of a Group A Coxsackie virus. Thus, it has been found to be ether resistant. It produces myositis in suckling mice typical of Group A infections. Myositis was produced by the direct inoculation of stool material into mice. The virus is cytopathogenic in tissue cultures, producing inclusions similar to those found in poliomyelitis and other enteric virus infections.[2]

Neutralization tests run both in this laboratory and at the New York State Laboratories in Albany point to a serological relationship between the Toronto virus and the prototype A16 virus. The two agents do not however appear to be identical, and further studies are in progress. The Toronto agent has been re-isolated on a number of occasions from the original specimens, and strains producing characteristic lesions in suckling mice have been shown to be identical to those isolated initially in tissue culture.

The isolation of this Group A Coxsackie virus from the stools of 79% of the patients tested suggests the possibility of an etiological relationship of virus to the clinical syndrome here described. This figure of recovery may be compared with the usual isolation rate of Coxsackie A viruses from the stools of normal persons and those with obvious non-viral illnesses, which does not usually exceed 5-10%.[42, 43] Group A Coxsackie virus type 16 has only rarely been encountered[15, 17] and has not apparently been isolated before on the North American continent. Parallel field studies performed at the time of the outbreak and during the summer of 1957 demonstrated the absence of this virus type elsewhere in the city of Toronto. Certainly, clinical illness of the type met with in the outbreak was limited to the housing estate and was not seen in two children's summer schools in the near vicinity. Further evidence of the causal significance of the virus is afforded by consideration of the child K.H., aged 9 months. Stool specimens taken from this young girl on July 16, 1957 were twice tested and found negative. She became ill on July 19; virus was isolated from a further specimen of stool obtained on July 20. Finally, a significant increase of serum neutralizing antibodies to the prototype A16 virus was detected in two patients.

The illness which has been described appears to constitute a new clinical syndrome, characterized by fever, ulcerative pharyngeal lesions, and a vesicular exanthem. As such the syndrome is quite distinct, but the less well developed forms of illness might be mistaken for certain commonly recognized clinical syndromes. The faucial ulcerative lesions might be described as herpangina, for they are similar in appearance to those described by Huebner.[22] However, in the Toronto illness, the gums and tongue were a not uncommon site of ulceration; it is rare for the lesions of herpangina to occur on the tongue or buccal mucosa.

The original description of herpangina by Zahorsky[55] has served as a sound basis for the clinical diagnosis of the condition, which we now attribute to infection with Coxsackie virus Group A. This has received ample laboratory confirmation. Zahorsky described the lesions as occurring on the posterior part of the pharynx; nevertheless, lesions of the tongue, gums, and hard palate have all been noted in association with Coxsackie Group A infections.[21, 22, 27, 34] A broadening of the term "herpangina" as defined by Zahorsky to include these anterior pharyngeal lesions may, however, limit its clinical usefulness, for it is evident from the careful studies performed by Parrott[40, 41] that without supporting laboratory evidence, the acceptance of lesions in the anterior part of the pharynx as part of the herpangina syndrome may falsely include herpetic, aphthous and other lesions not caused by Coxsackie A virus.

There were several features of the Toronto illness which differentiated it from herpes simplex. The Toronto illness was uniformly mild and of short duration. There were no lesions of the lips or in the peri-oral region; the oral ulceration was not severe, and there was no gingival hyperplasia, hæmorrhage or fœtor oris. Furthermore, the bullous lesion which was the most distinctive feature of the Toronto illness was constant in distribution, unlike an herpetic eruption; the clinical vagaries of herpes simplex are, however, well known.[5] Infection by herpes simplex has been excluded in the Toronto illness by the failure to isolate the virus from throat swabs and stool and also by the failure to demonstrate neutralizing antibodies in the sera of two patients who showed, in addition to the other features of the illness, well marked oral lesions.

The differential diagnosis of the Toronto illness from other short-term fevers which manifest a rash is shown in Table VI. Many of these illnesses are commonly seen in North America, whilst others are encountered only in the tropics. It can be seen from this table that an exanthem may occur in association with a Coxsackie virus infection, although this is uncommon. Kilbourne[26] described a morbilliform rash in a young girl from whom Coxsackie A9 virus was subsequently isolated. More recently, Gear[17] in South Africa described a roseolar rash on the abdomen of a patient which resembled the rash of typhoid fever, and which showed early vesiculation.

Infection with at least three of the serological types of Echo viruses has been associated with the presence of a rash, and in two instances pharyngeal lesions have been observed. Neva[35] has described

TABLE VI.—A COMPARISON OF THE MAIN CLINICAL FEATURES OF EPIDEMIC SHORT-TERM FEVERS WHICH MAY PRESENT WITH A RASH

	Maculopapular rash	*Morbilliform rash*	*Vesicular rash*	*Primary eschar*	*Ulcerative pharyngeal lesions*	*Koplik's spots*	*Aseptic meningitis*	*Polyarthritis*	*Lymphadenopathy*	*Splenomegaly*	*Leukopenia*	*Leukocytosis*	*Paul-Bunnell test*	*Conjunctival injection*	*References*
1. *Virus infections* Coxsackie group A	+		+		+		+							+	16, 17, 25, 38
Echo (4, 9, 16)	+	+	+		+		+							+	4, 6, 8, 12, 14, 24, 28, 29, 32, 33, 35, 36, 37, 39, 44, 46, 53
Boston exanthem	+	+			+										36
Rubella	+						+		+	+				+	
Measles	+	+				+					+			+	
Dengue	+	+							+	+				+	
West Nile fever	+		+						+	+	+				19, 30
Port Augusta fever	+						+								7
2. *Rickettsial infections* Rickettsialpox	+		+	+					+		+				20
Scrub typhus	+			+					+	+	+				
Murine typhus	+	+							+	+				+	
Boutonneuse fever	+	+		+					+					+	
South African tick bite fever and other forms of tick typhus	+			+					+					+	
3. *Bacterial infections* Leptospirosis	+						+		+			+		+	13, 31, 47
4. *Undetermined etiology* Infectious mononucleosis	+	+			+				+	+		+	+		
Roseola infantum (Exanthem subitum)	+										+				
Erythema infectiosum (5th disease)	+														
Murray Valley rash	+		+		+			+							1, 54

faucial ulcerative lesions comparable with the herpangina lesions investigated by Huebner,[22] and small buccal lesions were noted by Tyrrell.[53] In recent years, outbreaks of aseptic meningitis with a rubelliform rash caused by Echo type 9 have been described in different parts of the world. In one of the outbreaks described by Tyrrell[53] vesiculation was described, but this was slight in extent and unlike the lesions found in the present outbreak.

Differentiation of the Toronto illness from varicella can be made by the type of skin vesicle, and the absence of "cropping", pustulation and scabbing.

The more obvious differences between the Toronto illness and rickettsialpox are the absence of an initial skin lesion, the centrifugal distribution of bullæ, their superficial site in the skin, and the clear watery contents.

The leukocyte changes which occurred in the peripheral blood in the Toronto illness were similar to those described by Kilbourne in Coxsackie virus infections. The presence of large numbers of atypical mononuclear cells raised an early suspicion of infectious mononucleosis, but the Paul-Bunnell test was negative in three selected cases.

The occurrence of mild congenital lesions in four babies born at least six months after the onset of the outbreak of illness in the housing estate is brought to notice only as an observation. The congenital defects mentioned are common ones, and the mothers were not, as far as is known, taken ill during the early part of pregnancy. The possible importance of enteric viruses in the causa-

tion of congenital malformations must be borne in mind, however, and is worthy of further study.

SUMMARY

An outbreak of a febrile illness characterized by the presence of pharyngeal lesions and a vesicular exanthem, which affected 60 persons in the vicinity of Toronto during the summer of 1957, is described. The distinctive triad of fever, ulcerative lesions of the fauces and mouth, and a bullous eruption arising from a macular exanthem is considered to constitute a new clinical syndrome. The illness was in every case mild and admission to hospital was not necessary. There were no sequelæ.

The epidemiology of the outbreak is described. Fifty-two per cent of the members of the affected households became ill. The incidence of illness was highest in children of the one to nine year age group and it was considered that they introduced the illness into the family group. The high incidence of illness in this age group is explained by reason of their close contact at play and in particular through the use of small portable swimming pools.

Group A Coxsackie virus was isolated from a high percentage of the patients (71%). The virus showed some serological relationship to Group A Coxsackie virus type 16.

The isolation of this virus from 79% of the patients' stools suggested a causal relationship between it and the clinical illness described. This suggestion was given support by the demonstration of a specific antibody response to the related Coxsackie virus A type 16 in three patients, by the temporal relationship of virus isolation to the clinical syndrome in one case, and by the absence of illness or virus isolation in a control population.

The distinctive clinical features of the illness are compared with other short-term fevers which may be encountered in temperate or tropical climates and which may manifest pharyngeal lesions or an exanthem.

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RÉSUMÉ

Au cours de l'été 1957, 60 personnes vivant dans la banlieue de Toronto furent atteintes d'une fièvre accompagnée de lésions pharyngées et d'un exanthème vésiculaire. La triade fièvre, lésions ulcéreuses du gosier et de la bouche et éruption bulleuse faisant suite à un exanthème maculaire semble représenter un nouveau syndrome clinique. L'état des malades ne nécessita aucune hospitalisation et on n'observa pas de reliquats. D'après des relevés épidémiologiques, 52% des membres des familles affectées furent atteints. La plus grande fréquence se vit chez les enfants âgés d'un à neuf ans et l'on croit qu'ils furent le vecteur par lequel cette maladie s'introduisit dans les maisonnées. Le grand nombre de cas chez les jeunes s'explique par les nombreux contacts au jeu et tout particulièrement dans les petites piscines portatives.

On isola le virus Coxsackie groupe A chez la majorité des malades (71%). Ce virus déploya quelques affinités sérologiques avec celui du type 16. (Coxsackie groupe A). Sa présence dans 79% des échantillons de selles des malades suggère une relation de cause à effet entre le virus et l'affection clinique décrite plus haut. Cette suggestion fut appuyée par la démonstration d'un anticorps spécifique à ce virus Coxsackie groupe A type 16 chez trois malades; par la relation temporelle entre l'isolement du virus et la déclaration du syndrome clinique dans un cas, et enfin, par l'absence de symptome et de virus chez le groupe témoin.

Le tableau clinique de cette affection est comparé à celui d'autres fièvres de courte durée que l'on trouve dans les climats tempérés ou tropicaux et qui peuvent se manifester par des lésions pharyngées ou un exanthème.

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INJURIES TO THE SACRAL PLEXUS IN OBSTETRICS*

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INTRODUCTION

INJURIES to the peripheral nerves below or at the brim of the true pelvis have been reported subsequent to pelvic laparotomy, and after vaginal delivery. At laparotomy, the injury has been to the femoral nerve lying lateral to the psoas muscle and presumably due to pressure of retracting instruments on the nerve trunk. The obstetrical injury has involved the sacral plexus, resulting in foot-drop and sensory changes over the foot and leg. The latter complication of the puerperium is considered in this review.

The incidence of this complication of labour and delivery is low, as reflected by the reports in the literature. Chalmers (1949)[3] reviewed the literature and found 142 reported cases. More recently, Brown and McDougall (1957)[2] added 11 more cases over a nine-year period. Tillman (1935)[6] reported nine cases in 18,000 deliveries from the Sloane Hospital over a 10-year period. In this presentation 10 cases are reviewed from the Toronto General Hospital and four cases from other Toronto hospitals over the past five years. While the true incidence of the complication cannot be calculated from these reports, it is estimated that the incidence of some form of nerve injury may be about 1 in 2000 deliveries. As the nature of minor nerve trauma is transient and often overlooked, the frequency with which paralysis and sensory disturbances are clinically recognized in the puerperium must be about 1 in 5000 deliveries.

Von Basedow (1838) described the first case of foot-drop with sensory loss over the foot after forceps rotation and delivery of a large infant in deep transverse arrest. Since then the variation in the nomenclature of this neurological complication of labour and delivery has reflected the theories of its etiology. Neuritis puerperalis (Windscheid, 1899), traumatic neuritis of the puerperium (Tillman, 1935), maternal obstetrical palsy (Beattie, 1933; O'Connell, 1944), and peroneal nerve palsy (Mills, 1945) are but a few terms.

The etiological factors which are possible and which are excluded from the discussion in this paper include cortico-spinal vascular accidents, vitamin deficiency diseases and protrusion of an intervertebral disc (O'Connell, 1944).

The site of injury was first thought to be the sacral plexus, which was compressed by the fetal head. Bianchi (1867) and Hünermann (1892) further localized the nerve injury to the lumbosacral trunk where pressure on the trunk occurred as the fetal head descended through the brim of the pelvis. Brooks, and later Lambrinudi (1925), suggested that rotation of the sacrum during labour and the hyperextension of the lumbar spine produced a stetching injury to the lumbosacral trunk because it was a taut and relatively fixed nerve trunk. Smith has estimated from the work on laboratory monkeys that there is enough mobility to the trunk to prevent any traumatic stretch which might occur because of the few degrees of rotation of the sacrum during labour.

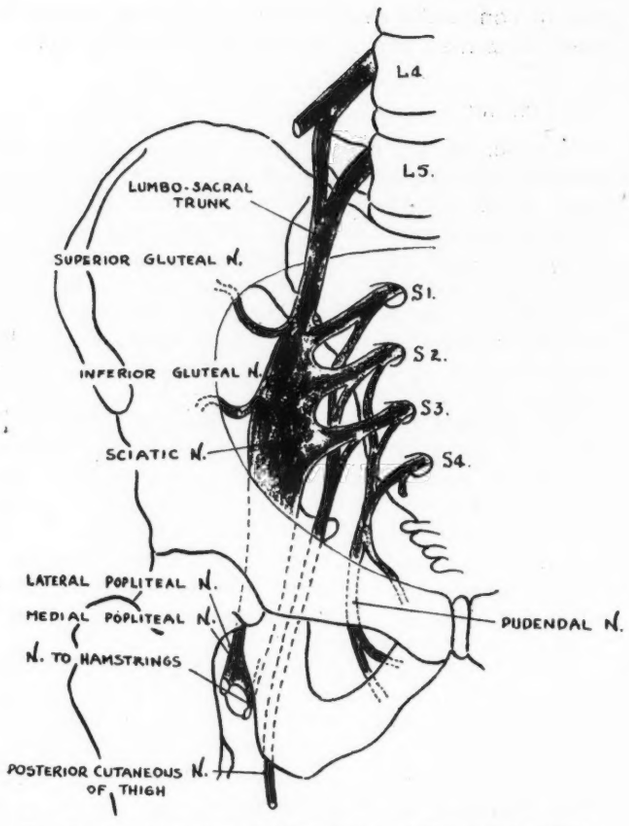

Fig. 1.—Components and distribution of the sacral plexus.

Kleinberg (1927) emphasized certain clinical features peculiar to obstetrical palsies; they were (a) disproportion, (b) prolonged labour and difficult delivery, and (c) instrumentation. Beattie (1933) suggested that injury to the pelvic nerves was caused by obstetrical forceps during difficult mid-pelvic operations.

ANATOMY

A brief review of the anatomy of the sacral plexus may facilitate the explanation of the mechanism of injury (Fig. 1). The sacral plexus takes origin from the primary undivided anterior rami of L. 4, 5 and S. 1, 2, 3. The plexus lies on the medial aspect of m. piriformis, as it leaves the pelvis through the greater sciatic notch. Although the pudendal and sciatic nerves form the two main terminal branches of the plexus, the sciatic nerve is readily divisible into three component parts: (1) the nerve to the hamstrings; (2) the medial popliteal nerve arising from the anterior division of the plexus and supplying the muscles of the

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morphological front of the limb; (3) the lateral popliteal arising from the posterior division and supplying the muscles of the morphological back of the limb, which include m. tibialis anterior, m. extensor digitorum longus and brevis, m. extensor hallucis longus, and m. peroneus longus and brevis. This muscle group probably derives the greater portion of its segmental nerve supply from the upper roots of the sacral plexus. Foerster has charted the sensory distribution of each nerve root and, while there is a major degree of overlapping, the relevant roots are: L.4, which supplies the medial aspect of the leg; L.5, which supplies the dorsum of foot and lateral aspect of the leg; and S.1, which supplies the sole and posterior aspect of the lower half of the leg (Fig. 2). Of special

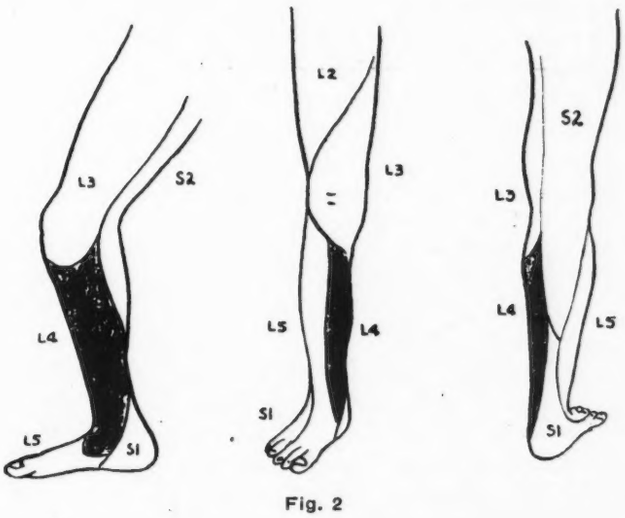

Fig. 2

interest is the lumbo-sacral trunk comprising fibres from L.4 which join the anterior ramus of L.5 on the ala of the sacrum. As the trunk crosses the brim of the pelvis it takes a lateral course over the sacro-iliac joint to join the sacral roots which make up the sacral plexus. The roots of L.4 and L.5 arise deep to the belly of m. psoas magnus, but as the lumbo-sacral trunk it slips from the protection of m. psoas deep only to the pelvic fascia, and lies relatively exposed over the sacro-iliac joint, until it reaches m. piriformis.

PHYSIOLOGY OF NERVE INJURY AND RECOVERY

In the literature, the name "traumatic neuritis in the puerperium" or "obstetrical palsy" is affixed to these cases of foot-drop due to obstetrical trauma. Russell Brain defines the nerve lesion as a perineural inflammation resulting in pain and impaired function of the nerve, due to compression of the nerve fibre by inflammatory œdema. The clinical onset, findings and recovery reflect the nature and severity of nerve damage. The usual nerve injury seen in the puerperium is of a type characterized by loss of conductivity of the axis cylinder without apparent break in the continuity of the nerve trunk. As the result of sudden or prolonged compression of the nerve, there is rupture of the myelin sheath of Schwann and escape of myelin into the endoneural spaces. The œdema of the nerve trunk and infiltration by inflammatory cells produce a transient impairment of nerve function. The nerve still retains its normal response to faradic stimulation distal to the site of injury, but in more severe injuries there is degeneration of the axon and loss of the normal faradic response. The peripheral nerves are mixed nerves and, as there is a varying degree of resistance of fibres to injury, motor and sensory recovery are not synchronous. The autonomic nerve fibres are most resistant to injury and recovery is rapid. Motor fibres are the least resistant to injury and the last to return to normal function. The rate and pattern of recovery depend upon the severity of the injury. Where the injury is of minor degree the muscles recover quickly as a group, but where axonal degeneration follows the injury, motor and sensory recovery proceeds more slowly in a serial order distally from the site of the injury.

CASE HISTORY

To illustrate this clinical entity, the most recent case history of peripheral nerve injury after labour is reviewed.

Mrs. McC., a 26-year-old, para i, gravida ii, white woman, was admitted to the Burnside Hospital in labour at 1 a.m. on March 12, 1957. Her prenatal course was uneventful and her first pregnancy had ended in normal delivery at term of an infant weighing 7 lb. 3 oz. She was 5′ 1″, weighing 164 lb., and on admission was having moderate five-minute contractions. The head was 2 cm. above the spines in the L. O. T. position and the cervix was 1½ fingers dilated. She was in strong labour throughout the day and received 400 mg. of meperidine (Demerol). Because of slow progress, in spite of good labour pains, the patient was x-rayed. Pelvimetry studies revealed a pelvis with a true conjugate of 10.5 cm.; the vertex was in the L. O. T. position, and the pelvis was considered adequate. At 6 p.m., after 20 hours of strong labour, the cervix was fully dilated, and the head still in the transverse position and 2 cm. below the spines. After an hour and 15 minutes in the second stage, the fetal head had rotated into the left anterior oblique position. The patient was given a general anæsthetic, and as Simpson's forceps could not be satisfactorily applied, Kielland's forceps were used to complete the delivery of a slightly depressed infant weighing 8 lb. 13 oz. On the second post-partum day the patient was febrile, and bed rest was continued. On the third post-partum day the patient stated that since delivery she had noted numbness over the dorsum of the right foot and great toe. Examination revealed paralysis of m. tibialis anterior, m. peroneus longus and the extensors of the toes. The remainder of the muscles of the leg were intact. There was diminished pin-prick, light touch and proprioceptive sensation over the dorsum of the right foot, extending up over the lateral aspect of the leg, in the cutaneous distribution of L.5. On the 7th post-partum day electrical testing of the

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muscles was carried out; while there was normal response to faradic stimulation in m. peroneus longus, there was no response in m. tibialis anterior or m. extensor hallucis longus. The electrical response suggests the development of reaction of degeneration. Treatment in hospital was by sedation and foot application of a foot board and night splint. The patient was discharged from hospital on the 11th post-partum day to be fitted with a spring foot-drop splint, and to be followed up at four-week intervals until the onset of peripheral nerve recovery.

In August 1957, she was seen again in the outpatient department. Muscle power had returned to m. tibialis anterior, and she complained only of weakness of the dorsiflexors at the end of the day. She had discarded her foot-drop spring splint after two months' use. Sensation was impaired for a small area over the lateral aspect of the dorsum of the foot, much decreased from the original area of sensory impairment.

MATERIAL

When lateral popliteal nerve palsies of metabolic, inflammatory, neoplastic or vascular origin, or those resulting from degenerative disc disease are excluded, the clinical features of traumatic obstetrical palsies are significant and worthy of consideration.

In keeping with Tillman's remarks, this obstetrical complication occurs most commonly in healthy young primigravidæ; 9 of our 14 cases occurred in this group, while 3 had had two deliveries and 2 three deliveries. In the multiparous group it was apparent that their previous infants were significantly smaller, with presentations which were not unusual and allowed labour and delivery to take place per vaginam without incident.

The combination of an unproven pelvis and a large baby always presents an obstetrical challenge, and the weight of the infants in this series tends to reflect the association of oversized infants with the occurrence of this complication. Of the infants 75% (11) weighed over 3400 g. and of these, one-third (4) weighed over 4100 g. For primiparæ, the average weight of the infants was 3750 g., which while not excessively large is greater than the average of 3200 g. for the newborn.

Infant weight and pelvic capacity must be considered together when abnormal labour due to bony dystocia is reviewed in individual cases. Stature bears a significant relationship to pelvic capacity, and in the series under consideration the average height of the patient was 60½" (151 cm.); thus the size of the infants born to these women must be considered to be in excess of their capacity for a normal labour. When there are a large baby, a patient of below average stature, and a small pelvis with some unfavourable features, obstetrical difficulties are almost certain.

While prolonged labour with a large baby may result in compression of the nerve, prolonged labour was not a feature in this group. Labour was less than 12 hours (Fig. 3) in over one-half the cases. In the three cases in which labour was prolonged over 24 hours, heavy sedation and malposition were etiological factors.

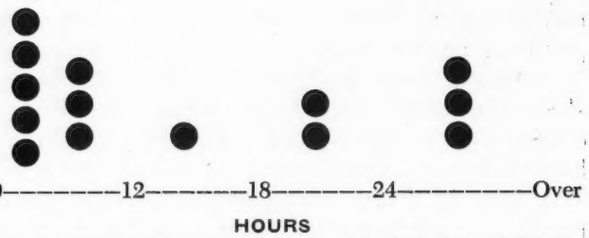

Fig. 3.—Distribution of 14 cases and duration of labour resulting in peripheral nerve injury.

In the remaining cases, with the exception of one case of absolute cephalo-pelvic disproportion, normal uterine action effected satisfactory progress of labour. This points out the insignificant effect on early labour of the bony features of the type of pelvis associated with obstetrical palsy.

Presentation, position and method of delivery are important features of our series. The position was abnormal in all but one case, the most frequent malposition being the occipito-transverse, which occurred in 9 cases. Other abnormalities included two cases of occipito-posterior presentation, one brow and one breech; another malpresentation was not recorded. The high incidence of malposition in the mid-pelvis suggests that the bony features of the pelvis interfere with the normal mechanism of rotation and descent during the second stage of labour, and accounts for the high incidence of mid-pelvic operations. In this series there were 10 mid-forceps and two low forceps deliveries, and one Cæsarean section. The difficulties in the mid-pelvis are reflected in the frequency with which manual and forceps manipulations (Table I) were carried out to effect rotation and delivery. Operations within the mid-pelvis are accompanied by a risk of serious injury to soft tissues, including the sacral plexus. Injury to the latter is estimated to occur in about 2 to 5% of mid-pelvis operations. The figure may be higher if one considers all the minor paræsthesiæ in the extremities seen in the puerperium after forceps deliveries.

TABLE I.—INDICATIONS AND OUTCOME IN TEN CASES OF MID-FORCEPS OPERATIONS, ALL FOLLOWED BY PERIPHERAL NERVE INJURY

Mid-forceps rotations, transverse arrest	8
A. Forceps attempted, manual rotation	2
B. Manual rotation attempted, followed by mid-forceps delivery	3
C. Forceps rotation successful, then forceps delivery	3
Forceps to the after-coming head	1
Mid-forceps, occipito-anterior	1

CLINICAL FEATURES

The clinical picture of nerve root injury usually appears immediately after delivery, although in three cases it was not recognized until after the 4th post-partum day. Of particular interest in regard to the mechanism of nerve injury is the case

of a primipara who experienced numbness radiating down the leg with rupture of membranes one hour before an assisted breech delivery with easy forceps application to the after-coming head.

Weakness of the leg was the major complaint, and the delay in making known this sequel to a difficult delivery is understandable. This complaint is often attributed to large painful episiotomy or an intramuscular injection; nonetheless, it may be an indication of serious injury to pelvic structures. Early ambulation tends to bring this weakness of the leg to the attention of the patient but, unless they are aware of the possibility of this injury, nurses and house staff may disregard this complaint. The sense of numbness, tingling, or pain in the foot and leg was present in some form in 85% of cases. The commonest complaint was numbness, usually in the lateral aspect of the leg and dorsum of the foot. Vasomotor dysfunction suggested by coldness in the toes occurred in one case. In no instance was there gluteal pain. Where pain occurred it was moderate, and in the two patients it was associated with numbness along the course of the sciatic nerve, not unlike true sciatica.

Impairment of sensation to pin-prick and light touch was present in 70% of cases, and in the remainder hyperalgesia was present; in each the sensory change was in the cutaneous distribution of L.4 and L.5. While all the modalities were not impaired, Russell Brain states that reduced proprioceptive sensation is the most constant finding.

Weakness or paralysis of m. tibialis anterior was a constant feature and is characteristic of L.4 and L.5 injury. The long extensors of the toes and peroneal muscles were involved in some of the more severe cases. In only one case was there weakness of the thigh muscles, suggesting injury to the sacral components of plexus. Reflex changes were of equivocal value in diagnosing the site of injury.

DIAGNOSIS

When abnormal labour and difficult delivery precede the onset of foot-drop, nerve root injury is highly probable. Neurological consultation is advisable to rule out the possibility of other causes of peripheral nerve palsy, and to confirm the diagnosis of traumatic neuritis.

The lumbar spines and pelvis were radiographed in nine cases; in three of these, pelvimetry studies were done in the puerperium. In no case was there evidence of degenerative disc disease in the lumbo-sacral region, which some writers feel to be a significant factor in the etiology of this injury.

While pelvic measurements are of value, the general conformity of the pelvis, and in particular the posterior pelvis, is more important. Cole (1946) and Tillat and Diemont (1947) pointed out some of the radiological features of the pelvis associated with nerve injury during labour. These include: (1) straight sacrum; (2) flat, wide posterior pelvis; (3) prominent sacro-iliac joint; (4) posterior displacement of the transverse diameter of the inlet; (5) prominent ischial spines; (6) wide sacro-sciatic notches.

When the posterior arc of the pelvis is flattened by a broad straight sacrum, the true conjugate diameter is borderline, and the greatest transverse diameter is displaced posteriorly; the fetal head tends to occupy the posterior pelvis. If the mid-pelvis is unfavourable because of the prominent spines, transverse arrest frequently follows. Tillman and Moloy have referred to the wide sacro-sciatic notch; this was not a striking features in this series, but another feature worthy of comment is the long posterior ilium and the prominent sacro-iliac joint. It is the latter feature which exposes the lumbo-sacral trunk to injury by a large fetal head or the obstetrical forceps, which further encroaches upon the capacity of the high mid-pelvis. While all these features were not present in each case, there was a combination of factors present whereby a large infant occupied the posterior portion of a pelvis with prominent sacro-iliac joints, thereby exposing the lumbo-sacral trunk to trauma. While cephalic-pelvic disproportion was present in one case, the pelves were considered adequate in most instances for babies of average weight. Only on review of the radiographs in the puerperium were the significant bony features appreciated as factors contributing to the occurrence of nerve injury.

MECHANISM OF INJURY

The high incidence of difficult mid-forceps operations, particularly for deep transverse arrests, suggests injury to nerve roots by the obstetrical forceps. Difficult forceps applications in the mid-pelvis are not infrequently accompanied by jerking of the leg when the anterior blade is being positioned. The lower edge of the anterior blade rolls over the lumbo-sacral trunk as the forceps crosses the sacro-iliac joint while being swept over the fetal face. Manual rotation is also implicated, but the flatter back of the hand or the fetal head impinging upon the nerve produces less trauma than the sharp blade of the forceps. It is not surprising then that a combination of manual manipulation and forceps application was carried out in 5 of the 14 cases in an attempt to reduce the trauma to soft tissues where deep transverse arrest occurred. The mechanism of nerve injury in the case of the breech is interesting in that root irritation followed rupture of the membranes. This suggests pressure on the nerve trunk by the greater trochanter or ilium of the breech; however, inasmuch as the pelvis was considered borderline and mid-forceps were applied to the after-coming head, trauma due to forceps application cannot be completely dismissed. In one case, spontaneous rotation from an occipito-posterior followed by a spontaneous delivery of a baby of average weight, after a short hard labour, resulted in foot-drop.

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While the injury to the lumbo-sacral trunk appears to be brought about by mid-pelvic manipulation of forceps, it is obvious that other mechanisms produce trunk injury in those cases not delivered by forceps. A large fetal head in the brim or rotating in the mid-pelvis in a few instances may produce a compression injury or vascular stasis and subsequent anoxic injury to the nerve trunk. It is known that œdema and inflammations of the tissues around the nerve may produce temporary dysfunction of the nerve.

TREATMENT

Treatment in the main is expectant and directed towards rest of the part and prevention of contraction deformities in the recovery period. In hospital, sedation, foot board, sand bags and night splints are used and on discharge a walking plaster or spring drop-foot splint is recommended. The drop-foot splint is to be used until there is return of function to the extensors of the foot, when more active measures to exercise the muscles of the anterior compartment of the leg are feasible. Physiotherapy was not carried out routinely in all cases. Hospital stay was not prolonged more than a day or two beyond the usual post-partum stay, for the discomfort in the leg was usually of short duration.

PROGNOSIS

While the literature states that the prognosis is always guarded, return of normal sensory function was usually complete within four weeks; occasionally, improvement was noted before the patient was discharged from hospital. Motor function was the last to return, but there was complete recovery in most cases within a maximum period of 12 weeks. At the end of six weeks, there was improvement in motor power to such a degree in some cases that the foot-drop splint was no longer required. When the onset of recovery of sensory and motor function is delayed for more than three months, and there is associated muscle atrophy, it is highly probable that there has been axonal degeneration. Muscle paralysis may be permanent, but improvement may be expected over a period as long as two years.

PREVENTION AND SUBSEQUENT PREGNANCIES

In the primipara with a small pelvis and average sized infant, the risk to mother and infant should be seriously considered before a difficult mid-forceps delivery is attempted, or labour terminated by Cæsarean section. Most obstetricians today would favour Cæsarean section under adverse conditions rather than risk a hazardous mid-forceps operation.

The management of subsequent pregnancies in an attempt to prevent injury deserves comment. Five cases have been delivered subsequently of smaller infants without sequelæ. One patient complained of numbness in her leg during labour, but in the puerperium no abnormality was found. Where there has been moderate nerve injury in a previous pregnancy, some authors feel that Cæsarean section is indicated in subsequent pregnancies. Those five cases delivered without event deserve attention, and the place of Cæsarean section should be reconsidered in prevention of this neurological complication. In all cases a trial of labour seems justified; it is particularly essential if the fetus appears to be smaller than the previous infant. The inaccuracies of clinical estimation of fetal size are well known, but, if labour is satisfactory and delivery from below anticipated with ease, the judicious use of forceps is permissible. While a trial of labour is justified before Cæsarean section, there is no place in the management of subsequent pregnancies for "trial of forceps" on a patient whose previous obstetrical history suggests traumatic lumbo-sacral trunk palsy.

SUMMARY

Fourteen cases of peripheral nerve injury due to obstetrical trauma and resulting in foot-drop are reviewed. The anatomical background and the mechanism of injury are suggested. The injury is to the upper roots of the sacral plexus, usually without disruption of the nerve axis. Primiparæ with large babies necessitating difficult mid-forceps delivery are likely to have this peripheral nerve complication. While the prognosis is guarded, recovery from foot-drop is usually complete in about three to four months, when the latter is managed simply with a drop-foot brace.

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RÉSUMÉ

L'auteur a colligé une série de 14 cas de lésion obstétricale du plexus sacré avec paralysie péronière et trouble de la sensation du pied et de la jambe. La fréquence de cette affection est diversement évaluée à un cas par 2000 ou par 5000 accouchements. Après avoir évoqué les différentes hypothèses étiologiques, l'auteur nous offre un rappel anatomique des nerfs du bassin.

Selon Russell Brain la lésion serait une inflammation périneurale qui causerait de la douleur et nuirait à la fonction par compression des fibres nerveuses par l'œdème inflammatoire. Il peut même y avoir rupture de la gaine de Schwann avec épanchement de myéline à l'intérieur du nerf. Les nerfs périphériques sont mixtes et ne recouvrent pas les deux aspects de leur fonction simultanément si bien que l'amélioration de la perception sensorielle peut ne pas aller de pair avec celle de la force motrice.

La lésion s'est vue surtout chez les jeunes primigestes. La présence d'un fœtus volumineux accompagné ou non d'une capacité pelvienne réduite a été notée. La durée du travail n'a pas semblé contribuer à l'étiologie dans cette série.

Par contre, l'auteur suggère que les reliefs osseux du bassin qui s'opposent à un mécanisme normal de rotation et de descente peuvent jouer un rôle soit par les complications qu'ils entraînent, soit par les manœuvres que l'on doit mettre en jeu pour les prévenir.

Les symptômes neurologiques apparaissent aussitôt après la délivrance. Les malades se plaignent surtout de faiblesse dans les jambes. Dans 85% des cas, elles accusent aussi de l'engourdissement, du picotement et de la douleur à l'aspect latéral de la jambe et au dos du pied. Des perturbations vasomotrices ont déjà été rapportées. L'examen montre de l'hypo ou de l'hyperalgésie à la piqûre dans les zones intéressées (L4 et L5). Dans la plupart des cas la paralysie disparaît au bout de trois ou quatre mois pendant lesquels la malade porte un support qui soutient le pied et permet aux extenseurs de regagner leur tonus.

HYPERSENSITIVITY MYOCARDITIS OCCURRING WITH SULFA-METHOXYPYRIDAZINE THERAPY*

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THE PURPOSE of this article is to report three cases of a morphologically identical, acute interstitial myocarditis, found at autopsy and believed to be of allergic nature. This condition was characterized by an accumulation of inflammatory cells throughout the heart muscle, with cardiac histiocytes and eosinophilic leukocytes predominating. Although these cells were scattered freely through the interstitial network of the myocardium, a certain predilection for the perivascular regions was evident. Nowhere was this process associated with a vasculitis.

The patients, all elderly men, had been hospitalized for a variety of conditions, but each one had developed a urinary infection for which a common treatment was given.

The myocardial changes evident in two cases appeared of such severity that they were assumed to be the direct cause of death. In the third case, the inflammatory changes present within the heart muscle were much milder and appeared relatively unimportant compared with the other findings at autopsy.

PERTINENT CLINICAL SUMMARY

CASE 1.—W.S., a 73-year-old retired painter, was admitted to Sunnybrook Hospital on September 22, 1957, because of a crushing retrosternal pain of recent onset. This pain had come on while at rest and was associated with dyspnœa and sweating. In addition there was nausea and vomiting. He had a history of several attacks of angina pectoris relieved by nitroglycerin tablets, and of recurrent bronchitis with emphysema and a lower urinary tract infection in 1954. The chest pain had rapidly subsided after admission, and a mild gastroenteritis had become evident. The physical findings included pulmonary emphysema, fine crackling basal rales bilaterally and a heart of normal size, functioning with a normal rate and rhythm, free of murmurs. The blood pressure was 115/60 mm. Hg. The liver did not appear enlarged and there was no ankle œdema. The clinical impression was that of arteriosclerotic heart disease with minimal failure and angina pectoris. Treatment consisted of a low salt diet, aminophyllin, Thiomerin, ammonium chloride and nitroglycerin. There was rapid clinical improvement with disappearance of all symptoms in a few days. Repeat urine examination, however, showed evidence of a urinary tract infection. Because a catheter specimen grew coagulase-positive staphylococci, treatment was further supplemented by sulfamethoxypyridazine (Kynex) (0.5 g. 3 times a day). This drug was given for a period of one week, starting from September 25. On October 2, the patient suddenly became febrile, confused, and dyspnœic at rest, and rales were again heard in the chest. In spite of oxygen, and penicillin and streptomycin (Penstrep, 2 c.c. b.i.d.), there was deterioration and death occurred on October 6, after a severe attack of cyanosis.

At autopsy many punctate, petechial hæmorrhages were found in the superficial, subepicardial fatty tissue mainly distributed along the coronary arteries. These changes were most pronounced in the region of the coronary sulcus. Similar but less marked ecchymoses were seen subendocardially in the left ventricular wall. Microscopically there was an acute interstitial myocarditis, characterized by a patchy infiltration of the interstices with eosinophilic leukocytes, polymorphonuclears, a varying number of histiocytes and fibrinous strands (Figs. 1 and 2). A moderately severe arteriosclerosis of the coronary arteries had produced slight focal myocardial fibrosis. Other findings of note were vesicular and bullous emphysema of the lungs,

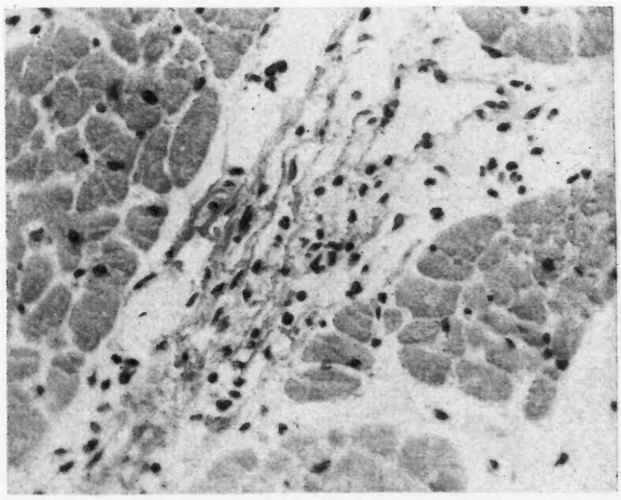

Fig. 1 (Case 1).—Interstitial exudation of fibrin (high-power).

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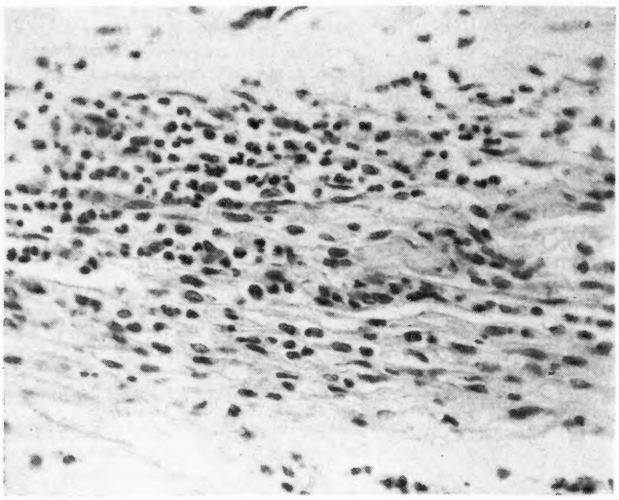

Fig. 2 (Case 1).—High-power view of interstitial inflammatory reaction with many eosinophils.

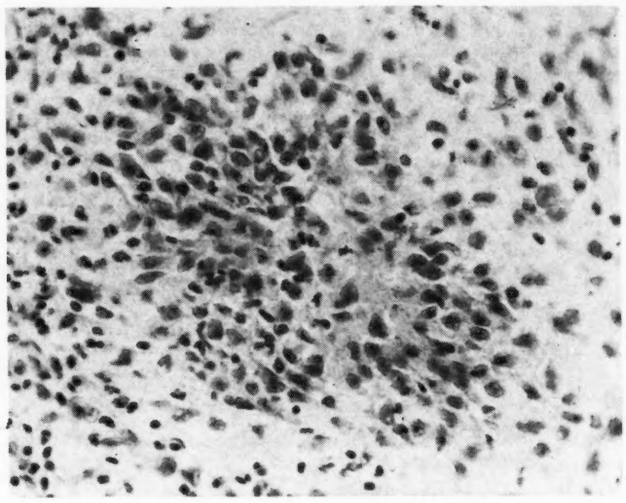

Fig. 4 (Case 2).—High-power view of interstitial myocardial granuloma.

generalized arteriosclerosis of moderate degree with nephrosclerosis and benign prostatic hyperplasia.

CASE 2.—W.H., a 68-year-old pensioned veteran, was admitted on September 4, 1957, because of a recurrent cystitis and urethritis. The cause of this infection was a urethral stricture sustained during World War I and resulting from shrapnel injury. Since 1945 this stricture had required regular dilatation. He had had a myocardial infarction in 1951, a transurethral resection of prostate with obliteration of a false passage, and a cholecystectomy for a chronic cholecystitis and cholelithiasis. On admission there was a heavy pyuria; urine culture grew *A. aerogenes*. Treatment consisted of a low salt diet, sulfamethoxypyridazine (0.5 g. b.i.d.), Furadantin, an indwelling catheter and bladder irrigations with normal saline. The initial clinical course was uneventful, the patient afebrile; the urinary sediment, although not bacteriologically clear, showed marked improvement. On September 26, approximately three weeks after admission, fever developed with temperatures ranging between 101° F. and 102° F. Simultaneously there were episodes of dyspnœa and bouts of left anterior chest pain. The electrocardiogram, taken at the time of this sudden change, showed a sinus tachycardia with a rate of 140 per minute and a left bundle branch block. On September 30, death occurred suddenly after an attack of severe dyspnœa and cyanosis.

Postmortem examination revealed a heart which, in addition to an area of fibrosis in the posterior interventricular septum, showed extensive subepicardial ecchymoses along the coronary vessels similar to those seen in Case 1. Microscopic examination showed a severe acute myocarditis with extensive interstitial infiltration by eosinophils. There were also granulomatous foci mainly composed of cardiac histiocytes and located predominantly in a perivascular fashion (Figs. 3, 4 and 5). Areas of granulomatous inflammation were also seen in the spleen, a lymph node and bone marrow. A trabeculitis was not observed in the spleen. Other autopsy findings included myocardial fibrosis, secondary to an old occlusion of the circumflex branch of the left coronary artery; vesicular and bullous emphysema of the lungs, chronic cystitis and testicular atrophy.

CASE 3.—A.T., an 85-year-old Boer War veteran, was admitted to the Sunnybrook Hospital on June 13, 1957, from a Toronto hospital for postoperative care after

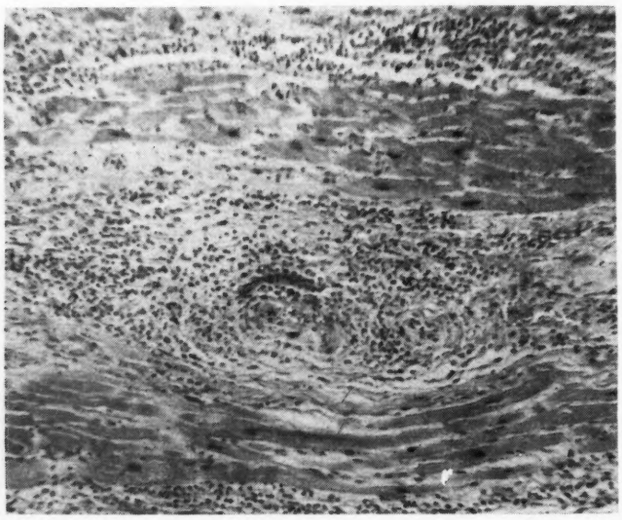

Fig. 3 (Case 2).—Low-power view of acute interstitial inflammation.

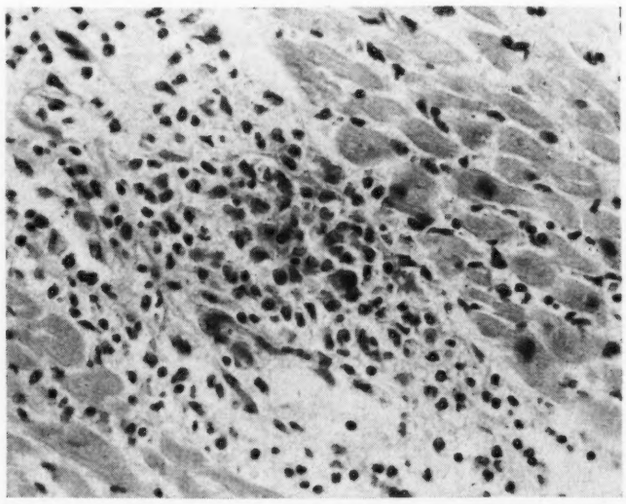

Fig. 5 (Case 2).—Acute interstitial myocarditis (high-power).

a transthoracic œsophago-gastric resection for an adenocarcinoma of the stomach. The immediate post-operative course had been stormy, with the development of a bronchopneumonia, which had required a tracheotomy. Congestive heart failure had further added to the complications and the delayed wound healing.

On arrival at the Sunnybrook Hospital, this pleasant and co-operative elderly patient showed gross pitting œdema of the lower extremities and a partially healed thoracotomy scar with a purulent sinus. Physical examination further revealed decreased air entry over the left lower lobe and moist rales at the bases. There was a palpable liver edge just below the right costal margin and also evidence of free fluid in the abdomen. Pus from the surgical wound grew coagulase-positive staphylococci, only slightly sensitive to chloramphenicol (Chloromycetin) and oleandomycin. The Hb. value was 62%, white cell count 6200 and E.S.R. 100 mm. in one hour. Treatment was directed towards controlling the congestive failure, and was supplemented with Chloromycetin (250 mg. 6 hourly). The initial hospital course was favourable, but slow deterioration soon ensued with signs of a progressive failure. Two months after admission a right hemiparesis developed. Skull radiographs showed the presence of a round calcified lesion attached to the falx and located in the left upper parietal region. Around the same time the patient started to complain of dysuria and frequency of urination. The urinary sediment contained a moderate number of pus cells, and heavy growth of *B. coli* was obtained on culture. On August 14, sulfamethoxypyridazine (0.5 g. twice a day) treatment was started. The patient's condition deteriorated more and more, and he became confused and at times short of breath. A low-grade fever developed and death occurred on September 8, 1957.

The main autopsy findings consisted of a recurrent adenocarcinoma in the region of the old resection line with involvement of adjacent lymph nodes and a meningioma of the left parasagittal area with compression of the motor cortex. Further significant findings included an acute bronchopneumonia and prominent generalized arteriosclerosis with fibrosis of the myocardium secondary to obliterative coronary artery sclerosis. The interstitial network of the myocardium was infiltrated with inflammatory cells, many of which were eosinophil leukocytes. Nowhere throughout the heart muscle was there evidence of recent necrosis of muscle bundles.

The acute myocarditis observed in these three patients had several features in common. The only common gross feature observed in Cases 1 and 2 was the presence of small subepicardial hæmorrhages, which were particularly prominent along the distribution of the coronary vessels. Microscopically there was a rich interstitial exudation with eosinophil leukocytes. Recent degenerative changes were completely absent and nowhere in the many sections examined was there evidence of vasculitis.

The intensity of the inflammatory reaction was most pronounced in the second case, where large aggregates of polynuclear cells were present throughout the interstitial tissue and particularly in the perivascular regions. Another prominent microscopic feature of this case was the granulomatous collections of cardiac histiocytes, which at places showed a typical radial arrangement. Similar granulomatous lesions were seen in the spleen, lymph nodes and bone marrow. In all these extracardial locations this change was accompanied by the presence of eosinophils. In Case 1 the inflammation was confined to the myocardium only, and here the exudation of fibrin was a conspicuous feature. Throughout the interstices, fibrinous material had produced a fibrillary network enmeshing the inflammatory cells. The granulomatous foci seen in the previously mentioned case were not apparent in Cases 1 and 3. The microscopic changes in the heart muscle of Case 3 were identical to those described immediately above, but less intense.

COMMENT

Since the onset of sulfonamide therapy, a number of reports concerning allergic manifestations towards these drugs have been published. One has only to study Simon's[1] extensive review of the literature up to 1943, to get an idea of the frequency and variety of lesions reported after administration of these drugs. Among the various types of lesions described, myocarditis has taken a prominent place. In a study of autopsy material at Ann Arbor, French and Weller[2] noticed a large number of cases with interstitial myocarditis, characterized by eosinophil cellular infiltrations for which the usual etiologic factors appeared to be lacking. After careful analysis of their material, they concluded that these changes were probably secondary to sulfonamide medication, the only factor known to be common to all cases. They were able to produce similar lesions, although more focal in nature, in experimental animals through the daily administration of various sulfonamides in doses comparable with the usual human dose in terms of body weight. The inflammatory changes in the heart muscle of patients were seen after a total dose of as little as 5 grams, but no lesions were found where the use of the drugs had been discontinued for more than 30 days before death. The microscopic findings consisted of a cellular infiltration of the interstitial network with large mononuclear cells of clasmatocytic type together with numerous eosinophils. More, McMillan and Duff,[3] in a study of 22 cases in which lesions were found attributable to sulfonamides, describe two morphologically different reactions in the heart muscle: granulomatous lesions and those characterized by an acute interstitial inflammatory reaction. The granulomata consisted of a closely packed arrangement of large mononuclear cells. Eosinophils, when present, were sometimes very numerous. Rich,[4] in a recent review, has emphasized that the hypersensitivity reaction can not only manifest itself as an ordinary inflammatory lesion, but also may take the form of a tuberculoid lesion with typical epithelioid and giant cells. Miliary foci of

necrosis were described by French[5] in many organs, among which were the spleen, lymph nodes and bone marrow. In his recent text on systemic pathology, Saphir[6] describes the myocarditis found in so many hypersensitivity reactions as a specific entity, characterized usually by the presence of many eosinophils, although occasionally allergic granulomas can be found within the heart muscle.

The profound eosinophilic character of the lesions found in our three cases strongly suggests a hypersensitivity reaction induced by a drug. This impression is further strengthened by the close histologic similarity between these changes and those described by others. After careful perusal of the hospital records it became evident that all three patients had received sulfamethoxypyridazine, a sulfonamide compound of relatively recent development. The only other drug given in common was chloral hydrate but, considering the known sensitizing properties of sulfonamides, particularly in reference to the development of an allergic myocarditis, it is only reasonable to assume that the sulfamethoxypyridazine was responsible for the myocardial changes. We believe that it is also significant that all three cases occurred within a relatively short period of time, and that identical lesions in the heart have not been found in this hospital before.

SUMMARY

Three cases are presented of an acute interstitial myocarditis of a type seen in drug-induced hypersensitivity reactions. Characteristic morphological features were the presence of many eosinophils and allergic granulomas. All patients received treatment with a relatively new sulfonamide compound, sulfamethoxypyridazine. It is believed that this drug was the responsible etiologic agent.

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RÉSUMÉ

Les auteurs présentent trois cas de myocardite interstitielle aiguë comme on en voit dans les réactions médicamenteuses d'hypersensibilité. Au point de vue morphologique les lésions étaient caractérisées par de nombreux éosinophiles et granulomes allergiques. Au cours de leur traitement, ces malades avaient reçu un sulfamide d'origine assez récente, la sulfaméthoxypyridazine. Les auteurs sont portés à croire que ce médicament est l'agent étiologique responsable des troubles décrits plus haut.

DIVERTICULUM OF THE FEMALE URETHRA—AN OVERLOOKED CONDITION*

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DIVERTICULUM of the female urethra has been, in the past, so rarely diagnosed by the individual doctor that any informative presentation of the subject must largely be a compilation of the experiences of many interested observers.

Eleven cases of this condition are listed in Ottawa Civic Hospital records from 1925 to 1957. No doctor has operated on more than two cases. However, the long history of some patients (in one case over 20 years), the frequent story of repeated admissions for cystoscopies and gynæcological consultations, and the previous diagnoses of recurring cystitis, urethral stricture, urethrocele, and Gärtner's duct cyst, reveal that the condition had in many instances been previously overlooked by the gynæcologist, the urologist, and the radiologist.

Similar conditions are the rule elsewhere. The Cleveland Clinic reported seven cases in the 22 years preceding 1943, and 38 cases in the next ten years. Te Linde[8] claims that though the condition was described in 1805, it had frequently been overlooked at Johns Hopkins Hospital, where only 30 cases had been diagnosed from 1890 to 1949. Ten years ago the rate had risen to about one per year. Then the staff was alerted; soon eight cases per year were detected, and now a case is diagnosed every week.

If urethral diverticula are in reality so common, why has the gynæcologist not been finding them when he opens the anterior vaginal wall? Campbell,[6] describing his technique for vaginal hysterectomy and referring to the mobilization of the bladder, stated that "great care should be taken in this step of the dissection as not infrequently a small diverticulum of the bladder is present which may easily be cut or torn across." Urethral diverticula tend to run upwards beneath the bladder. Diverticulum of the female bladder is rare (two women in 151 cases, according to Lower). There is little doubt that Campbell with his large experience of vaginal hysterectomy was fairly frequently encountering early urethral diverticula over 15 years ago.

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Badenoch[1] states that it is doubtful whether the condition is ever congenital. It is very rarely found in children or the nulliparous, and is usually associated with a pregnancy or an obstetrical injury. All the Civic Hospital patients were married and all but one had had children. Menville and Mitchell, quoted by Herbut,[5] in analysing 80 cases in 500,000 admissions to the Charity Hospital of Louisiana, found that most of the patients were married and had borne children. The ages ranged from 20 to 65, with an average age of 38.8.

SYMPTOMS

Very early cases may present no symptoms. In the Civic Hospital cases, presenting symptoms included frequency of voiding, often extreme, and sometimes with stress incontinence due to the accompanying cysto-urethrocele; difficulty in voiding; pain on voiding, varying from a distressing burning in the urethra to a suprapubic ache over the bladder; painful intercourse; a swelling in the vagina, in one case so great as to require a Cæsarean section; and in one case arthralgia, presumably due to the focal infection.

DIAGNOSIS

An appearance of "tumefaction in the suburethral tissues" (Curtis) aptly describes the condition. A red, tender, doughy urethrocele must be regarded with suspicion. Sometimes a definite cystic mass may be made out—quite small, or large enough to extend up to the anterior fornix. Pressure on the mass may, if its urethral opening is adequate, cause purulent or cloudy fluid to escape from the meatus. These classical findings, as in other conditions, are those of late cases. Of 12 diverticula recently detected at Johns Hopkins Hospital, only two were associated with a palpable suburethral mass. The sole physical finding may be tenderness in the neighbourhood of the urethra.

Urethrography is a valuable diagnostic aid. Formerly the tip of a Foley catheter was tied off just beyond the balloon and a hole cut in the main channel an inch (2.5 cm.) from it. With the catheter inserted, the balloon inflated, and tension applied to the catheter, radiopaque fluid injected could not enter the bladder and might fill a diverticulum. A successful outcome with this technique, employing 4% sodium iodide, is shown in Fig. 1. However, this technique failed in Case 2. Pinching the labia tightly around the catheter, or constricting the meatus with an Allis forceps if the patient is anæsthetized, has been recommended. An attempt was made in Case 2 to occlude the urethral orifice with a salpingography acorn slipped back along the catheter. This also failed because of leakage, as the catheter is not round. Possibly applying thick glue or rubber cement to the catheter before sliding the acorn against the meatus might stop the leakage. Drs. Davis and Cian,[2] gynæcological residents at Johns Hopkins Hospital, appear to have

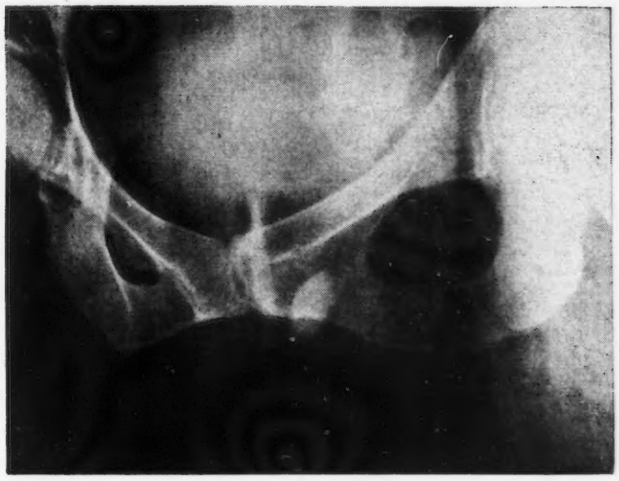

Fig. 1 (Case 1).—A diverticulum filled with contrast medium is shown to the right of the catheter.

solved the problem by sliding an inflatable balloon up against the meatus. This device* has greatly increased the number of cases of urethral diverticula detected at this hospital. After practising the inflation of the balloons *with air* and determining the inflation necessary to immobilize the sliding balloon, the double balloon catheter is inserted. The bladder balloon is inflated, and traction is applied to close the upper end of the urethra. The urethra is stripped digitally to evacuate urine or pus. The contrast medium† is then injected till it begins to escape at the meatus. The second balloon is then slid up

*Double balloon catheter No. 187, 14F, C. R. Bard Inc., Summit, N.J., U.S.A.

†Umbradil, Astra Pharmaceutical Products, Inc., Worcester, Mass., U.S.A. (Xumbradil in the U.S.A.)

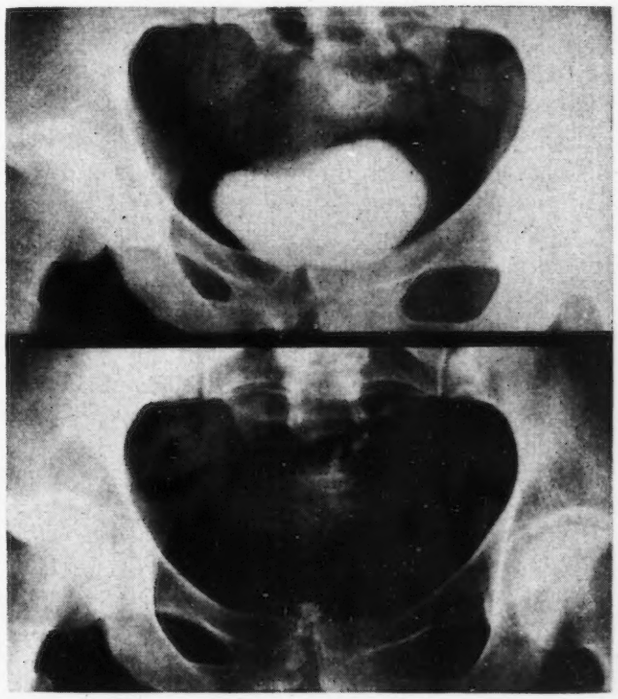

Fig. 2 (Case 2).—Upper—1946: A shadow at the symphysis in a woman with cystitis was mistakenly regarded as an extra centre of ossification. Lower—1955: Shadows had increased to three, and acute suburethral swelling revealed the true diagnosis.

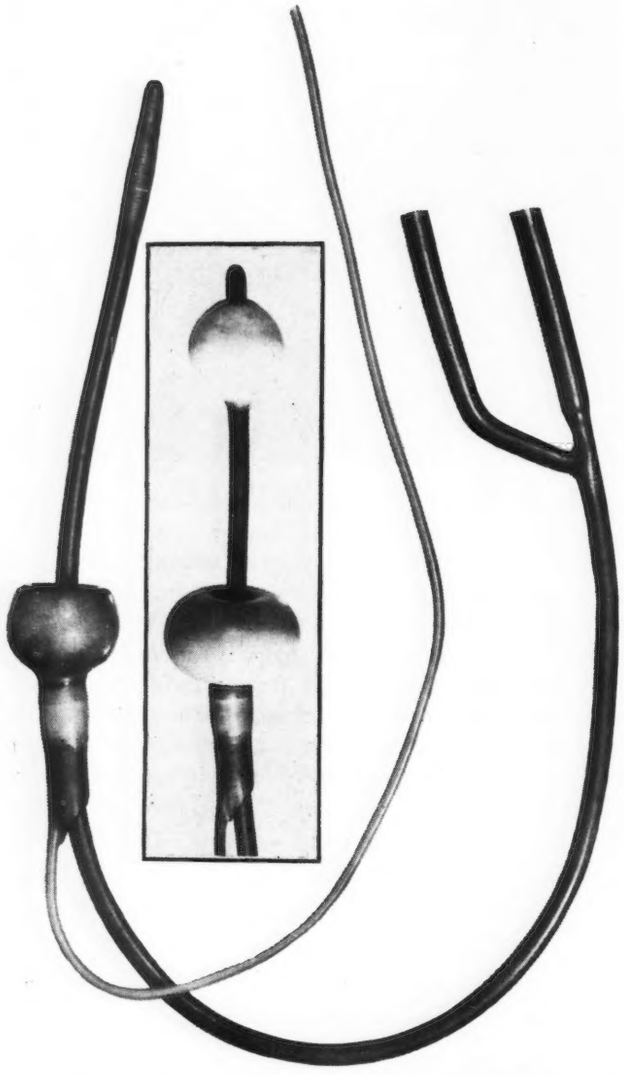

Fig. 3.—The Davis and Cian modified Foley catheter for urethrography. Centre: The bladder balloon has been inflated and the orifice balloon slid forward and inflated.

to the meatus and inflated. Traction may now be released. A further injection of 3 to 4 c.c. is usually sufficient to distend the urethra and the diverticulum. The patient is now ready for x-ray examination. Davis and Cian centre the cone over the symphysis with a 30 inch film-focal distance, and use 70 to 80 milliampere-seconds at 52 to 62 kilovolts. Their machine has a 5 to 1 grid. An antero-posterior view is taken. If any urethral sacculations are shown, this is followed by an oblique view. The catheter is then removed and a final antero-posterior view taken.

The urethra may then be examined with the McCarthy panendoscope. As it is withdrawn along the urethra with the water running, the dark orifice of the diverticulum may be seen, from which the milky Umbradil may be seen escaping. The orifice may be small and may even be occluded and impossible to find, or it may be as large as 1 cm. in diameter. Multiple openings have been described. Rarely one has been found in the roof of the urethra. Most orifices are in the distal two-thirds of the urethra.

With the above technique, 12 cases were found at Johns Hopkins Hospital in as many weeks.

TREATMENT

If the diverticulum has been detected early and is not causing symptoms, no treatment is necessary. However, the patient should be told of her condition.

Treatment is essentially surgical. In advanced cases, a course of treatment, prolonged if necessary, in an attempt to reduce inflammation and œdema would appear advisable before surgery is undertaken. Hot sitz baths, short-wave diathermy, daily emptying of the sac by digital pressure and the use of sulfonamides or antibiotics may be tried. Any method which would reduce the tissue reaction in advanced cases is worth considering, even the use of cortisone.

OPERATIVE TECHNIQUE

The diverticulum is approached through an incision in the anterior vaginal wall.

In early cases without much hard œdema the classical textbook illustration shows the diverticulum being shelled out, apparently as simply as a ganglion at the wrist, or being peeled out like a hernia sac. It has not been so simple in most of the Civic Hospital cases.

Some authorities have endeavoured to localize the suburethral cavity by endoscopically introducing a ureteral catheter into it. Moore, once the cavity has been incised, introduces a Foley catheter (with its tip off), surrounds it with a purse string suture and blows up the bag. The main incision is then made and divides to include the purse string. Traction on the catheter helps in dissecting out the sac.

In extensive cases where the inflammatory mass extends up under the bladder, the entire anterior vaginal wall is opened as for cysto-urethrocele repair, by making a transverse incision above the cervix and slitting up the anterior wall almost to the meatus. The flaps are dissected laterally in the usual way. Dissection of the suburethral and subvesical mass may be extremely difficult and time-consuming and the tissue may have to be removed piecemeal with here and there a fragment of the lining of the cavity. A guide in the urethra is essential—preferably a solid one such as a metal catheter or male sound. The hole in the urethra is repaired with a purse string if small, or by interrupted sutures of 000 chromic catgut which must not penetrate the mucosa. The fascia is then approximated with two layers of interrupted chromic sutures and the vaginal incision closed.

ILLUSTRATIVE CASES

CASE 1.—J.E.N., a 37-year-old mother of three, was admitted complaining of frequency—sometimes up four times a night, pain in the left hip, and painful intercourse. There was a history of five hospital admissions

in the past nine years with cystoscopic examinations for cystitis. On examination there was an exceedingly tender mass along the left of the urethra, pressure on which caused pus to escape from the meatus. Urine culture grew a micrococcus and *Streptococcus viridans*. The patient was given sulfisomidine (Elkosin). On cystoscopic examination the panendoscope revealed a small opening in the urethra just below the internal sphincter. A urethrogram made with a tied-off Foley catheter (with an opening made 1 inch from the balloon) and using 4% sodium iodide, outlined a diverticulum (Fig. 1).

At operation a Foley catheter was inserted, midline incision was made and the diverticulum was visualized. It dissected free with difficulty and was removed in fragments, the urethra being opened in the process. The urethra was closed with interrupted 00 chromic catgut, and the fascia and vaginal wall were closed. The vagina was packed with gauze, which was removed in two days. The catheter was removed in eleven days.

The patient has been entirely relieved of her complaints.

CASE 2.—N.M.G., a 47-year-old mother of one child, was admitted on March 17, 1955, complaining of great difficulty in voiding, a painful swelling at the vulva, and pain in the groins. She had a long history dating back to 1934, when she was admitted for stricture and cystitis and was cystoscoped. In 1938, a bladder stone was removed and she was referred for gynæcological consultation. The anterior fornix was reported as obliterated. A second consultant regarded this as a congenital condition. In 1946 she was under treatment for stricture of the urethra. No stone was found on cystoscopy. At this time a shadow at the symphysis was reported as an extra centre of ossification.

On examination, what appeared to be a cysto-urethrocele was red, œdematous and doughy to the feel. Diverticulum was suspected and a small sound, introduced along the urethral floor in an attempt to enter it, grated on a stone. Radiography now revealed three shadows in the symphysis area. On an oblique plate with a catheter *in situ* the shadows were reported as 1 cm. below the catheter.

Sitz baths were ordered for relief, and as the urine was loaded with pus cells, tetracycline (Achromycin) was started. The patient was cystoscoped and the urethra examined with the panendoscope. The dark opening of the diverticulum was readily visualized at the junction of the upper and middle thirds of the urethra.

Operation.—Reversed Trendelenburg posture. A male sound was placed in the urethra and the perineum held up with a Sims speculum. The anterior vaginal wall was completely opened as for cysto-urethrocele repair. Hard œdema extended up to the cervix.

The lower part of the diverticulum was soon entered and the sound visualized. The upper part containing the stones was encased in a dense mass of chronic inflammatory tissue absolutely confluent with the bladder wall. The greatest care had to be exercised in searching for the cavities in this tissue lest the bladder be damaged. Bleeding was considerable—a brain suction tip was employed. Finally the third stone was found. The urethra was closed over the sound, the fascia approximated and the vaginal wall closed. The operation took four hours and the patient received two bottles of blood.

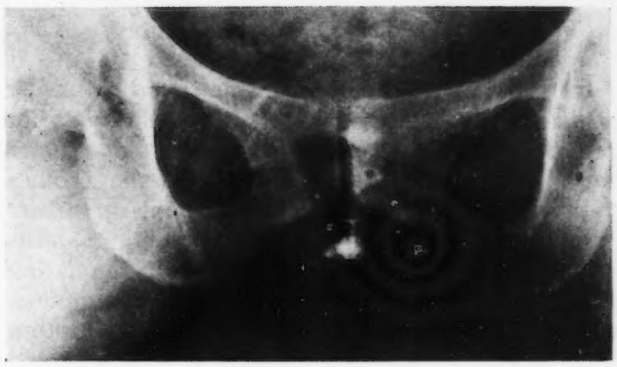

Fig. 4.—A urethrogram made with the two-bulb catheter by Drs. Dardick and Sternik warrants a tentative diagnosis of diverticulum in a woman with urethrocele, recurring pyuria, and local distress after voiding. The balloons are filled with air for better contrast and localization.

A Foley catheter was inserted and the vagina packed with iodoform gauze.

The long-standing periurethral inflammation in this case had produced a stricture of long standing. The patient has been followed up for three years and is symptom-free but requires monthly dilation of the urethra with a size 8 Hegar dilator (equivalent to a 24F sound).

NEWER SURGICAL TECHNIQUES

Ellik[4] states that: "The most simple, turgid, uninfected, and distally located diverticulum can be a delicate operative problem. In the most difficult cases the diverticulum may be concealed and closely enveloped by the vaginal vault and may be difficult to see as well as hard to mobilize. Surgical ablation may be accompanied by qualms, tedium, and hazard on the part of the operator—the sac was often disrupted and the residual pouch lost in a bloody quagmire."

He therefore revived, modified, and improved the old operation of incision and packing with gauze as practised by Cabot and by Furnis, who first destroyed the lining by fulguration. This sometimes required a secondary closure of a resulting fistula.

Ellik's technique.—The patient is placed in the reversed Trendelenburg posture. If the diverticulum is collapsed it is delineated by a small blunt hook (a bent probe will do) introduced through the urethra. The projection is grasped by two Allis forceps and a short stab incision made between them. After any fluid escapes, the sac lining is grasped by Allis forceps and the cavity is flushed with hydrogen peroxide. The inner lining is then excoriated thoroughly with a minute gauze sponge held in mosquito forceps. The cleansed and abraded cavity is then stuffed (not too tightly) with strips of oxycel gauze ¼ inch or slightly wider. The oxycel acts as a patch over the urethral ostium. *The small incision is then closed* with interrupted chromic sutures. The Foley catheter is left in seven days. The oxycel becomes

assimilated into a general pattern of fibrosis. Ellik claims seven cures by this technique.

Edwards and Beebe[3] locate the diverticulum by a direct urethral approach. After the anterior vaginal wall has been fully opened, as for major cysto-urethrocele repair, they slit up the urethra to the opening of the diverticulum, going no further than the junction of the upper and middle thirds to avoid damaging the bladder neck. Granulating edges are trimmed, and multiple openings unified, and the diverticulum is dissected out. The urethra is approximated over the catheter with interrupted submucosal sutures of 000 chromic catgut, the fascia is approximated, and the vaginal wall closed. The Foley catheter is left in for eight days. Five cases have been successfully treated with this technique.

RESULTS

Krieger and Poutasse after considerable experience at the Cleveland Clinic report the results of surgery as good. Rarely a urethro-vaginal fistula may require a secondary repair, and rarely a difficult case may require a second operation, the recurrence presumably being due to incomplete removal.

SUMMARY

Diverticulum of the female urethra has been often overlooked.

The patient with recurring pyuria, distress in voiding, and what is apparently a urethrocele, may have a diverticulum. A new technique for urethrography is greatly facilitating its detection.

The classical treatment is surgical removal—the earlier the easier. Edwards and Beebe suggest an approach by splitting the urethra.

As an alternative to a difficult dissection, Ellik advises a return to the simpler method of incision and packing, which he has improved.

Indebtedness is acknowledged to Dr. J. Victor Berry, senior surgeon, Genito-urinary Division of the Department of Surgery, and to Dr. Douglas W. Cockburn, Assistant Director of Radiology, Ottawa Civic Hospital, for their co-operation in this study.

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RÉSUMÉ

On a tendance à oublier que l'urètre féminin peut être porteur de diverticules. La malade qui accuse de la pyurie périodique et de la dysurie et dont le tableau clinique évoque la présence d'un urétrocèle peut avoir un diverticule. Une nouvelle méthode d'urétrographie a rendu le dépistage de ces lésions assez facile. Le traitement classique repose sur l'exérèse chirurgicale (le plus tôt sera le mieux). Edwards et Beebe suggèrent un abord qui consiste en une incision longitudinale qui s'étend jusqu'à l'ouverture du faux passage. Comme alternative à une dissection laborieuse Ellik recommande le retour à une technique plus simple et qu'il a améliorée, d'incision et de méchage.

THE STATUS OF PHENYLBUTAZONE (BUTAZOLIDIN) IN THE TREATMENT OF RHEUMATIC DISORDERS

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THIS STUDY was undertaken to determine the therapeutic value of phenylbutazone in a wide range of rheumatic conditions and to establish its position in relation to other anti-rheumatic drugs, keeping in mind the degree of relief obtained and the incidence of complications.

PHYSIOLOGY AND PHARMACOLOGY

The mode of action of phenylbutazone is not clearly understood, but experimental work has shown that the drug has analgesic, antipyretic, antihistaminic, uricosuric and anti-inflammatory properties.[1, 2] Absorption from the gastro-intestinal tract is rapid and complete, peak plasma levels occurring about two hours after oral administration and six to ten hours after intramuscular injection.[1] The drug is slowly metabolized in the body, about 20% of the administered dose disappearing in 24 hours and the drug having a half-life in man of approximately 70 hours.[3] At doses of 800 mg. daily the plateau plasma level is only slightly higher than at doses of 400 mg. daily. There is little to be gained therefore by the administration of larger doses, which greatly increase the hazard of toxicity.

RESPONSE TO THERAPY

Two hundred and seventy patients on phenylbutazone therapy have been seen and followed up by the author during the past year. Many gave a history of other forms of therapy — gold, steroids, etc., but phenylbutazone was not given to any who had an adequate response to salicylates. It will be noted in Tables I and II that the response in different rheumatic disorders varies widely. Patients who experienced major improvement had prompt and

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TABLE I.—RESPONSE TO TREATMENT

Diagnosis	*Major improvement*	*Moderate improvement*	*Poor or no improvement*	*No. of patients*
Gouty arthritis	75%	20%	5%	24
Ankylosing spondylitis	65%	26%	9%	23
Osteoarthritis	43%	22%	35%	58
Rheumatoid arthritis	36%	16%	48%	86

almost complete relief of pain and stiffness, which could be maintained on a small maintenance dose. Those classified as moderately improved had less relief, but felt that the therapy was well worth while, and wished to continue, sometimes in spite of minor complications. In those with a poor response the drug was discontinued after seven days.

TABLE II.—RESPONSE TO TREATMENT

Diagnosis	*No. of patients*	*Major improvement*	*Moderate improvement*	*Poor or no improvement*
Disc syndrome	12	4	4	4
Tendonitis	11	5	—	6
Bursitis	25	4	2	19
Episodic rheumatoid arthritis	1	1	—	—
Psoriasis with rheumatoid arthritis	2	2	—	—
Palindromic	2	2	—	—
Hæmophilic arthritis	2	2	—	—
Paget's disease	2	2	—	—
Costen's syndrome	2	2	—	—
Calcaneal spur	1	1	—	—
Post-herpetic neuralgia	5	3	1	1
Osteitis condensans ilei	2	1	1	—
Acute bunions	1	1	—	—
Reflex dystrophy	1	—	—	1

Relief of pain and stiffness usually occurs at from one to three days after administration, and if no improvement is obtained in one week the drug should be discontinued. When the drug is stopped there are no withdrawal effects, but symptoms return in a few days.

GOUTY ARTHRITIS

In this group, as in those reported by others, acute gouty arthritis responded more dramatically and more consistently to phenylbutazone therapy than any other rheumatic disorder. The effective oral dosage in acute gouty arthritis is 200 mg. three times daily until the acute symptoms subside, and then 100 mg. two or three times daily for a week.

Most patients respond dramatically, and within a few hours of oral administration the acute symptoms begin to subside. Toxic effects are rare because of the short period of administration. In those suffering from frequent acute attacks the administration of 100 mg. daily will often prevent recurrence. In those with less frequent episodes the drug may be used repeatedly when attacks occur, with apparently little if any danger of acquired sensitivity.

In this series 95% of patients experienced a satisfactory response, which is superior to our results from oral colchicine. When the diagnosis is in doubt, colchicine with its specific action has the advantage of providing a diagnostic test, but undesirable gastro-intestinal symptoms frequently follow its use. In observations on 520 gouty patients Kuzell *et al.*[4] obtained a good or fair response in 91% of those treated with phenylbutazone and in 80% of those treated with colchicine. Robins *et al.*[5] also consider phenylbutazone superior to colchicine because of the freedom from unpleasant side effects.

Phenylbutazone would appear to be the drug of choice in gouty arthritis, being equal to oral colchicine in effect and with less gastro-intestinal irritation.

ANKYLOSING (MARIE-STRUEMPELL) SPONDYLITIS

A surprisingly good result from phenylbutazone therapy in those suffering from ankylosing spondylitis has been reported in other studies[1, 5-7] and was confirmed in this group. As a rule, after two or three days of treatment, pain, stiffness and muscle spasm diminish with increased spinal mobility. In this study (Table I) the 90% favourable response obtained with phenylbutazone in spondylitis is in striking contrast to the result in rheumatoid arthritis where some 50% received benefit. It is interesting that the two patients with a poor response were women.

These findings and those of others suggest that phenylbutazone should replace x-ray therapy when such treatment is necessary in ankylosing spondylitis. This opinion is supported further by the reported incidence of leukæmia in those treated with more than one course of x-rays where "the observed deaths are probably at least 9 times those expected to occur".[8]

In a long-term comparison study of cortisone, ACTH and phenylbutazone in spondylitis, Holbrook[7] observed a 95% failure rate at the end of four years in those on cortisone and ACTH. In striking contrast, improvement on phenylbutazone was maintained in all but 4%.

The response reported in Table I confirms the opinion of others that, if drug therapy other than salicylate compounds is required in the management of ankylosing spondylitis, phenylbutazone is the drug of choice.

DEGENERATIVE JOINT DISEASE—OSTEOARTHRITIS

Although this treatment in degenerative joint disease is far less effective than in gout and spondylitis, phenylbutazone therapy was found to be worth while in about 60% of patients with peripheral and spinal osteoarthritis.

Most of these patients had distressing osteoarthritis in the hips or knees, and in such cases a trial of phenylbutazone therapy is indicated if less toxic measures of treatment have failed or relief by surgery is contraindicated. However, as Toone[1] has pointed out, the treatment of degenerative joint disease is a long-term project and patients affected usually belong to the older age group who may be more susceptible to toxic side effects.

RHEUMATOID ARTHRITIS

In this group about 50% of the patients felt that phenylbutazone was worth while in helping to control their symptoms. The value of the drug in certain patients was best demonstrated by those who have continued on maintenance doses for periods up to four years, have stopped, and have then started again because of the relief obtained. The percentage of patients with rheumatoid arthritis who maintain prolonged major improvement on a safe daily dosage is small but the possible value of phenylbutazone in an individual patient may be determined in seven days, at which point it may be continued or discarded. It should be clearly understood that phenylbutazone does not suppress the disease nor does it prevent progression of joint destruction. However, in comparison with long-term steroid therapy the side effects are less hazardous, the failure rate over years is less marked, and the problem of withdrawal effect is absent.

The patient suffering from rheumatoid arthritis must first be placed on a basic program which includes rest, proper exercises, local heat and adequate doses of salicylates. If this conservative program fails and the disease continues to progress with increasing severity and deformity, the use of additional therapy should be considered and a choice made from gold, steroids, phenylbutazone or chloroquine. Any beneficial effect from gold or chloroquine will likely not be obvious for six to twelve weeks. In the meantime, if increasing pain and stiffness is a problem, a trial with phenylbutazone is indicated for one week, after which, if no benefit is obtained, the drug should be discarded in favour of other measures.

Favourable results were obtained in episodic rheumatoid arthritis, psoriasis with rheumatoid arthritis, and palindromic rheumatism (Table II), but the number of patients was too small for a strict evaluation. In patients with psoriasis the skin lesions were not aggravated, and the presence of psoriasis is not a contraindication to the use of phenylbutazone.

DISC SYNDROMES

Twelve patients with cervical or lumbar disc lesions were given phenylbutazone for the relief of acute pain. Eight patients had worth-while relief and the drug was discontinued when the acute phase subsided.

TENDONITIS

The effect of phenylbutazone on bi ipital tendonitis, tennis elbow and De Quervain's disease was disappointing, less than 50% responding favourably. Local injection with hydrocortisone and oral steroid therapy is more beneficial in these lesions. In De Quervain's disease surgery is more often the treatment of choice.

BURSITIS

Twenty-five patients with acute or chronic subacromial bursitis were given phenylbutazone for the relief of pain and limitation of shoulder movement. Here also the result was disappointing, only six having major or moderate improvement. The injection of the bursa with hydrocortisone, followed if necessary by oral administration of steroids, is the treatment of choice for this condition.

HÆMOPHILIC ARTHRITIS

Two patients with hæmophilic arthritis, one with severe joint damage, obtained major relief from acute episodes of pain with phenylbutazone. One patient developed bleeding into a joint four days after cessation of therapy, which was probably due to the usual cycle of the disease.

PAGET'S DISEASE

The effect of phenylbutazone on the pain of Paget's disease was striking, major improvement occurring in both patients. If the pain of this disease does not respond to drugs with less toxicity, a trial with phenylbutazone for one week is indicated.

COSTEN'S SYNDROME

This temporomandibular joint syndrome is most often due to malocclusion of the teeth which may cause severe pain and limitation of mandibular movement. Treatment necessitates correction of the bite, a difficult procedure when pain and spasm exist. Two patients had marked relief from pain with phenylbutazone, which also facilitated dental treatment.

POST-HERPETIC NEURALGIA

This painful malady has been resistant to most forms of medication. Out of five patients treated with oral phenylbutazone, three had major improvement and one obtained moderate relief. This result would appear to be superior to other forms of therapy suggested in the past. In a series of eleven patients reported by Partelides[9] no failure occurred after five or six intramuscular injections of phenylbutazone, and it was stated that oral administration is not as effective as the intramuscular route.

OSTEITIS CONDENSANS ILEI

One patient had major and one moderate improvement. Here again, if the pain fails to respond

to drugs with less toxicity, a trial with phenylbutazone is indicated.

DOSAGE AND ADMINISTRATION

The severe toxic reactions reported in early papers were frequently associated with higher doses than are now employed. With a lower dosage schedule, the toxic reactions have shown a significant decline with no apparent impairment in therapeutic effect.[1] As mentioned above, the response to the drug should occur within one week, and if it is not worth while the treatment should be discontinued. Most physicians now use a dosage schedule of 600 mg. daily for two days, 400 mg. for two or three days, and then a maintenance dose of 100 to 300 mg. daily. A daily maintenance dose of 200 mg. is usually sufficient to maintain a constant therapeutic blood level. In this series, particularly in spondylitis, 100 mg. daily has been sufficient in a few patients.

In eight cases of duodenal ulcer, and in one following operation for carcinoma of the stomach, phenylbutazone was given in the form of suppositories, each containing 250 mg. The result from suppositories was equal to that from oral administration, but cessation of therapy was necessary in two patients, because of œdema in one and bloating and constipation in the other.

TOXICITY

Although the incidence of toxic reactions has been reduced by a lower dosage schedule they are still sufficiently common to demand close clinical observation of the patient on phenylbutazone therapy. Reactions are not likely to occur until after seven to ten days, so that short-term therapy as in acute gouty arthritis and bursitis is relatively safe.

TABLE III.
COMPLICATIONS OF PHENYLBUTAZONE THERAPY

Total number of patients	270
Patients with one or more side effects	27%
Major side effects	2.2%
Drug discontinued because of reaction	8%

The majority of complications appear before the twelfth week. This interval between the first and twelfth week is the critical period as far as toxic reactions are concerned.[2] In this series of 270 patients 27% had one or more side effects, most of which were minor and transient in nature (Table III). The major reactions occurring in 2.2% were pulmonary œdema in two, hæmorrhage from a duodenal ulcer in one, severe dermatitis in one, severe vomiting in one patient who later was found to have carcinoma of the liver, and hepatitis in one patient who later was found to have diffuse collagen disease. None of these major reactions was fatal.

Therapy was discontinued because of side effects in 8% (22 patients). Thirteen had gastrointestinal complaints, five had salt retention with œdema, three had dermatitis and one had severe headache. The total number of major and minor complications is shown in Table IV. Nausea was the most common complaint, with occasional vomiting and diarrhœa.

TABLE IV.—COMPLICATIONS OF PHENYLBUTAZONE THERAPY

Gastro-intestinal		Dermatitis	
Gastric irritation	23	Rash	16
Vomiting	3	Stomatitis	3
Diarrhœa	5	Lethargy	7
Irritation of ulcer	3	Headache	4
Hæmorrhage	1	Epistaxis	3
		Dizziness	4
Fluid retention with œdema		Palpitation	2
Peripheral	10	Confusion	2
Pulmonary	2	Swollen salivary glands	2
Face	12	Blood	1

Phenylbutazone may cause a significant retention of sodium chloride producing water retention with œdema, decrease in urine volume and increase in weight. The œdema is most pronounced on higher levels of dosage and often disappears completely when the lower maintenance dose is reached. This initial retention of fluid may cause a temporary drop in red blood cell count and hæmoglobin value by hæmodilution and should not be interpreted as a toxic effect on blood or bone marrow.

The great majority of skin lesions are slight and disappear rapidly when the drug is discontinued. In this series there was only one case of severe dermatitis in which the patient continued therapy after the onset of the rash.

HÆMATOLOGIC STUDIES

Because of previous alarming reports on the possible effect of phenylbutazone on the blood and bone marrow,[10] complete blood studies were carried out at three to four week intervals on the patients who received the drug for more than two weeks. The blood work was done by one technician who was aware of the problem and searched for any abnormality.

Two hundred and sixty-eight blood studies were made, including hæmoglobin determinations, red and white cell counts and smear examinations. In no case was any abnormality found which prompted discontinuing the drug. A few minor fluctuations in Hb. value occurred, but there was no indication of agranulocytosis, thrombocytopenia or aplastic anæmia. In one patient (Table IV) who had been on 400 mg. daily for 18 months, a toxic granulation was found in the cytoplasm which was considered to be due to a chronic genito-urinary infection resistant to antibiotics. One patient had been on maintenance therapy for over four years, seven patients over three years and thirteen patients over two years. Nevertheless, fatalities due to toxic reaction on the bone marrow have been reported. Kersley and Mandel[11] observed agranulocytosis with depression of all marrow elements in a pa-

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tient who received the drug for only 17 days at a dose never exceeding 400 mg. daily. They felt that routine white cell counts were useless and that warning the patient to report malaise, fever, and sore throat was a more important precaution.

SUMMARY

If additional medication other than less toxic salicylate compounds is found to be necessary, phenylbutazone is the drug of choice in the treatment of ankylosing (Marie-Strümpell) spondylitis. In gouty arthritis, phenylbutazone is at least equal to, and in some reports better than, oral colchicine, with less gastro-intestinal irritation. In rheumatoid arthritis, rheumatoid arthritis with psoriasis, osteoarthritis, disc lesions and some other miscellaneous rheumatic disorders reported above, a trial of phenylbutazone should be considered and the drug discarded if no relief is obtained in one week. In post-herpetic neuralgia the results appear to be superior to those with previous forms of therapy, but a larger study is required.

The majority of complications were minor and transient in nature, and the major reactions subsided on cessation of therapy.

The danger of toxicity is reduced by close clinical observation of the patient and prompt withdrawal of the drug at the first sign of reaction. Phenylbutazone should be avoided in patients with a history of peptic ulcer, hypersensitivity, or congestive heart failure. The lowest possible maintenance dose should be used, and the drug discontinued if no improvement is noted in seven days. In this series of patients, blood studies revealed no toxic effect from the drug on blood or bone marrow.

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RÉSUMÉ

Si la conduite du traitement exige un autre médicament que les composés moins toxiques à base de salicylate, la phénylbutazone est le choix par excellence dans la spondylarthrite ankylosante de Pierre Marie. Dans l'arthrite goutteuse, la phénylbutazone s'est montrée égale sinon supérieure à la colchicine *per os* avec cependant moins d'irritation gastro-intestinale. Dans la polyarthrite chronique évolutive avec psoriasis, les rhumatismes chroniques dégénératifs, les lésions discales et d'autres formes d'arthrite décrites dans le texte on peut se permettre l'essai de la phénylbutazone à condition de ne pas insister si aucune amélioration ne s'est manifestée après une semaine de traitement. Les résultats obtenus dans la névralgie post-herpétique semblent meilleurs que tout ce que l'on a vu jusqu'à présent, mais ils demandent à être vérifiés par l'analyse d'un plus grand nombre de cas.

La majorité des complications qui ont surgi au cours du traitement furent passagères et de peu d'importance; les réactions sérieuses disparurent dès que le médicament fut supprimé. Une surveillance étroite du malade avec interruption immédiate du traitement au moindre incident diminue les risques de réaction toxique. Il est préférable de ne pas employer la phénylbutazone chez des malades ayant des antécédents d'ulcus, d'hypersensibilité ou d'insuffisance cardiaque. Dans ces cas comme dans ceux décrits plus haut, il convient d'adopter la plus basse dose d'entretien possible et cesser au bout d'une semaine si l'amélioration espérée ne s'est pas produite. Dans la série de 270 malades sur laquelle porte cet article, on n'observa aucune répercussion toxique sur la moëlle ou sur le sang.

"DURAFOAM"—A NEW MATERIAL FOR REST SPLINTS IN THE PREVENTION OF DEFORMITY IN THE CHRONIC RHEUMATIC DISEASES

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THERE IS NO SPECIFIC CURE at the present for rheumatoid arthritis. It is all important, therefore, to prevent or correct any deformity that may lead to the tragedy of crippledom. The Canadian Arthritis and Rheumatism Society have calculated that the annual loss of wages through disability of the chronic rheumatic diseases is in excess of $75,000,000 (Dominion Bureau of Statistics, figures for 1951). This paper is concerned with a new material that can be used to help prevent some of the disablement in these diseases.

Deformity in rheumatoid arthritis develops in two stages. The most obvious is joint destruction. But even earlier than that can be detected, muscle spasm, the reflex mechanism to minimize pain by limiting movement of a painfully swollen joint, has insidiously started to lead to deformity. This spasm, though perhaps helpful to the joint, is ultimately harmful to the muscle itself by limiting movement and so leading to the wasting of disuse. This is particularly true during the night when the joints are pulled into deformity by powerful flexor muscles that cannot at that time be consciously controlled. Thus deformity becomes inevitable unless corrective measures are applied, especially at night.

This has long been recognized and various types of splints have been devised to offer a "spasm substitute"—one that would rest the joint satisfactorily, but at the same time avoid damaging the muscle and so avoid atrophy.[1] Until recently, plaster of Paris was the chief medium used for this purpose, but unfortunately it has many disadvantages, chief of which is the messiness involved in its use. Both doctor and patient require protective clothing, and

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the skin with its hair and nails becomes clogged and stuck together. In a recent assessment of plaster of Paris casts Simmons pointed out that the strength or durability of such casts was perhaps the most important property and that a great number of cast failures result from damage in the first 24 hours.[2]

Plastic materials have also been tried. They, too, have many disadvantages. They are expensive to make, since much time is taken up in making a model on which to mould the plastic and then fitting the plastic around it. This is usually because the plastic medium is either too hot to apply to the skin directly or some of the chemicals are toxic during the setting process. Frequently the resins used lead to dermatitis on the hands of the technician, so that few technicians are willing to expose themselves to them.

Certain combinations of plaster impregnated with resins have also proved unsatisfactory chiefly from the viewpoint of toxicity to the skin.

A search for more suitable materials has therefore continued in the attempt to find one that would fulfil the chief criteria for supportive splints: (1) lightness; (2) strength; (3) ease in making, applying and removing; (4) washability; (5) attractiveness. Recently DuraFoam has become available for clinical trial. This has proved very satisfactory. Its use has also led to some new techniques of splint-making referred to as "pre-design".

The basic principles of DuraFoam splinting consist in the use of a rapidly setting plastic foam inside a plastic envelope which is then cut out into a pre-designed shape and applied to the body where a quick final hardening results in a contour-fitting, light splint.

There are thus two essential components of a DuraFoam splint: the DuraFoam plastic material itself and a specially designed envelope. The DuraFoam is formed in a jar (or special dispensers—see below) by the interaction of two chemicals to form a non-toxic foam. This semi-solid foam is then poured into a transparent plastic envelope. One side of this envelope has a resilient coating; on the other, the film side, may be traced a variety of possible splint designs (Fig. 1). This is the principle of "pre-designing" and will be referred to again later.

The envelope lining on the one side has a dual function. Firstly it acts as a heat distributor during the application to the body while a small amount of heat is being generated in the foam; this helps to make the final splint cool in summer and not cold in winter. If a skin-tight fitting is required, the DuraFoam can be safely applied without the lining, if a little delay is allowed, as the heat is not great and quickly dissipates. Secondly, the elastic softness of the lining makes it very comfortable to wear, and by its very nature absorbs some of the variation in the size of the limb during the pattern of swelling change.

PRE-DESIGNING

The envelopes are available in several sizes appropriate to the length of arm, leg, neck or trunk. On one surface of each can be traced a variety of designs so that anterior, posterior or gauntlet type splints may be made. A set of celluloid basic patterns is available which can be laid on the envelope for the rapid tracing of these designs. New ones, of course, can be devised by the operator. Once the foam has been poured into the envelope and has been smoothed out by rolling, the design is easily cut around with ordinary scissors to the correct shape for the particular purpose. The splint is then moulded on to the body. It is held in position by an ordinary tensor bandage for a few minutes and when that is removed, the splint has been made.

The lining materials are available in several colours, as is the DuraFoam itself. Thus, the final product will have a very attractive one-colour appearance or may even be two-tone!

MODE OF SUPPLY

The material is supplied either as a complete kit or as a separate envelope with a DuraFoam dispenser. The kits consist of an envelope with its coloured lining and enough DuraFoam in two small jars to fill it. The dispenser contains a large quantity of both the ingredients along with the colouring material. The correct amount of DuraFoam is supplied by "dialing" the appropriate figure on the dispenser and holding the envelope underneath.

APPLICATION TECHNIQUE

The size of the envelope with its coloured lining is selected according to the size of the limb and the purpose of splinting. An envelope suitable for an arm is shown in Fig. 1, which also shows the design that has been traced on the side opposite to the lining. The appropriate design having been chosen, the envelope is test-fitted to check that the margins of the selected design actually accommodate the entire portion of the arm to be splinted. If this is not done before the material is cut out, the estimated design may turn out to be too small.

The two chemicals are then mixed either with an applicator in a jar (having separate kits) or mechanically in the dispenser. The chosen colours are added during this process. After about one minute, the foam caused by chemical action begins to thicken, as can be felt by the resistance to the stirring. The foam is then ready to pour into the envelope. If any should spill, no harm or erosion will take place, but as the material is sticky at this stage, it should be removed quickly with acetone because later it will be more difficult to do so.

After the foam is in the envelope, the whole envelope should be rolled once with a roller to spread the material smoothly and evenly.

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A FIFTEEN-MINUTE OPERATION

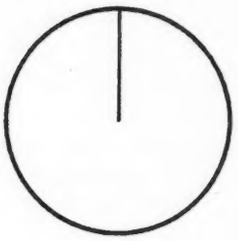
Lapsed Time

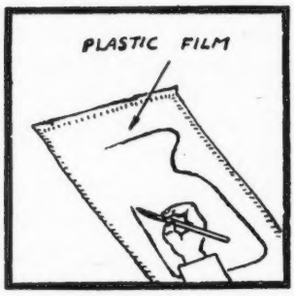
Diagrams

Select envelope to suit application.

Trace pattern on plastic film of envelope using a free-rolling ball-point pen.

Select kit of sufficient capacity to fill envelope.

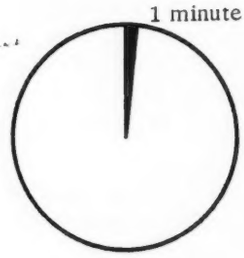


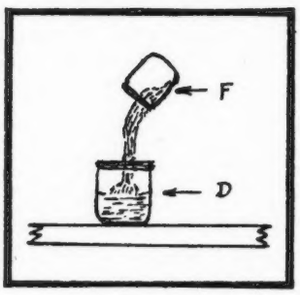


1 minute

Pour contents of container F into container D. Using spatula provided, be sure to scrape all of material from container F into container D.

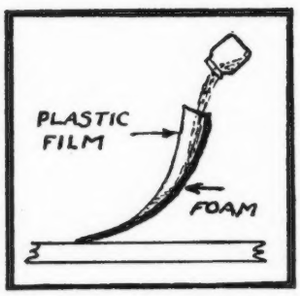
Using spatula, mix the combined materials in container D vigorously and thoroughly for approximately one minute or until a faint warmth is felt in the container.





2 minutes

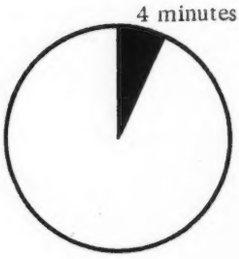
Hold envelope open with bottom of foam side resting on table and pour mixture into the envelope, allowing it to slide down over the foam surface inside the envelope as indicated in the opposite diagram. Use spatula to scrape all of the mixture from the container into the envelope.

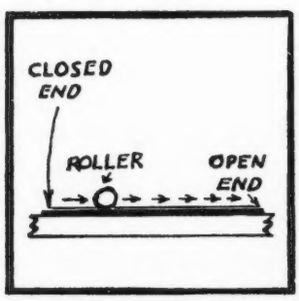


4 minutes

Lay envelope flat on the table and, using roller, roll the mixture over the length of the envelope once or twice to spread the material evenly through the envelope to a uniform thickness. Always roll from bottom of envelope towards the open end as indicated in the opposite diagram.

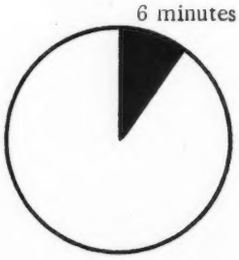
After rolling, allow material in envelope to set for approximately two minutes before cutting out pattern.

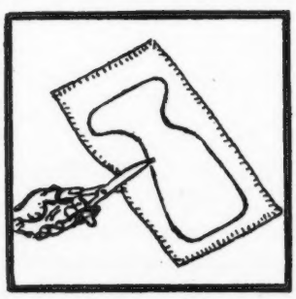




6 minutes

Make test cut in envelope with shears; if material is found to be slightly tacky, allow a few moments more to set, clean tacky material from shears with acetone, and cut out pattern along pre-drawn pen-line.

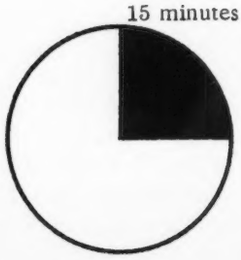




15 minutes

Place pattern on patient with foam side next to skin; pre-shape pattern to limb with hands, smooth out any wrinkles which may develop, and make snug fit to limb by wrapping with a bandage. A bandage of some non-stretchable material such as flannel affords a much smoother surface.

Allow cast or splint to harden for approximately nine minutes and remove forming bandage. With point of pen-knife loosen outer plastic film at a corner of the cast or splint and peel off, leaving a clean, hard, attractive-appearing surface.



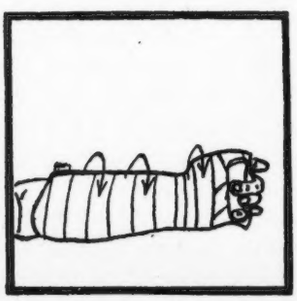


Fig. 1

After another minute or so, the foam is ready to be cut into its final shape. The test cut should be made with ordinary scissors at some point, and if the material is not tacky, as shown by the blades cutting cleanly, the design should be cut out.

The splint is then ready to apply to the body. It is wrapped around the part concerned with the lining side inwards to act as a buffer and pressure padding. An ordinary tensor bandage is adequate to secure the necessary amount of pressure to keep it in position till complete hardening takes place. This follows in a few minutes, the test of setting being when tapping on the side reveals that it is firm, a fact that can be corroborated by the "hard" noise emitted. The bandage can then be removed, revealing a rigid, closely fitting, light, attractive splint.

The splint can then be fastened in several ways. A broad latex, elastic strap can be attached to a single central dome which acts as an anchor to the strap as well as the fastener; or a broad cotton or plastic band or similar colour to the splint can be attached to the distal end and wound around it, to be finally tucked in at the top or secured by pressure-sensitive tape.

If some trimming is found to be necessary, the edges can be very quickly smoothed with sandpaper. More extensive trimming can be done by any light jig saw or plaster saw, should one want to reduce the size of the splint because of the patient's progress.

Many advantages of this material are listed in Table I. Some of them warrant special comment.

TABLE I.—ADVANTAGES OF DURAFOAM

1. Light.
2. Comfortable.
3. Snug-fitting.
4. Not messy, no protective clothing required.
5. Stronger by weight than other plastic.
6. Rapidly setting, yet easily moulded without cracking.
7. Can be re-modelled later if heated.
8. Washable, water-proof and buoyant.
9. Can be made under water.
10. Unaffected by oil, ointment, alcohol or secretions.
11. Not flammable.
12. Transparent to x-rays.
13. Insulated and thus cool; not hot, not clammy.
14. Shock-resistant and resilient; will not crumble.
15. Non-toxic.
16. Allergy-free.
17. Attractively coloured.
18. Inexpensive.

The chief of these is lightness. It is very important when making a splint to the limb where muscle wasting has taken place to ensure that the splint is not so heavy that it is an onerous burden to carry. Orthopædic hand splints have been known to weigh as much as 2 lb. Even the lightest plastic plaster units weigh about ½ lb., whereas a similar DuraFoam splint weighs only 2 oz. and yet does not sacrifice strength.

Another outstanding feature of DuraFoam is the absence of mess in its application. Plaster requires

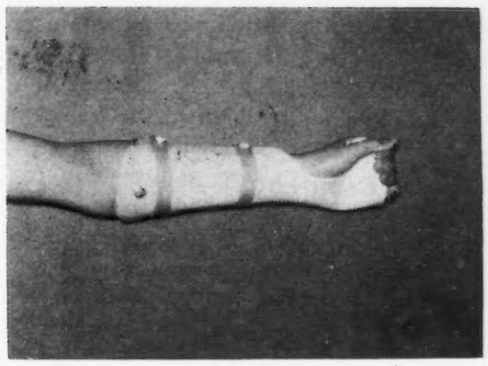


Fig. 2

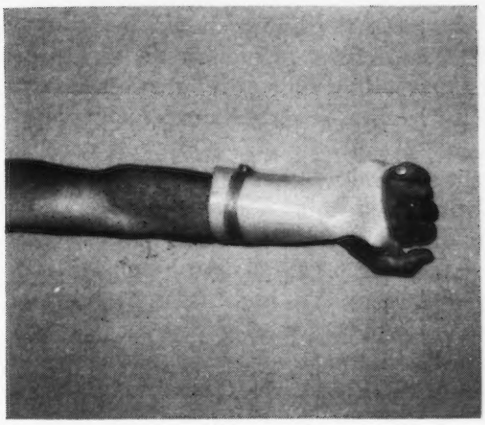


Fig. 3

Figs. 2 and 3.—Finished anterior and posterior splints showing a method of fastening to the arm with latex straps.

protective clothing and covering for both patient and operator. Even then the skin of both often requires the application of Vaseline to prevent the plaster sticking to hairs and under nails. DuraFoam makes no mess at all and can be prepared and applied without any danger of damaging, destroying or dirtying either clothes or skin. This is an obvious advantage and means that doctors, physiotherapists, occupational therapists and plaster room technicians will be more willing and ready to apply preventive, corrective splints. Splints can be made in the home at the bedside or even in the living room without any risk of causing a mess.

The fact that DuraFoam is transparent to x-rays is of great importance. When corrective splints of plaster are applied to children with hip arthritis, not only are they usually thick and heavy, but also a greater exposure to x-ray is required when checking on the condition of the joint. This is to be avoided, particularly to the pubic region of a growing child. DuraFoam permits the taking of a radiograph with no greater exposure than if no splint were there at all, without sacrificing detail of the film. It therefore avoids the necessity of taking off the splint, which would perhaps have to be done should a plaster splint be used.

Another way in which DuraFoam is superior to plaster is in its ability to take up a new shape after re-heating. Thus, as deformities are progressively

corrected, the new position can be retained by repeated moulding of the splint. The heat from an infra-red lamp or heating pad is sufficient for this purpose; or, more conveniently the splint may be placed in an ordinary kitchen oven at a temperature of 250 degrees for a few minutes. This obviates the necessity of making fresh plaster casts and so saves the time of the operator and various costs.

Because DuraFoam is waterproof and washable, it can be kept fresh-looking and clean. This is of importance in hip and leg casts, particularly in children, where secretions can be the source of unpleasant odours and a distasteful appearance. After washing, the lining should be squeezed free of water and then placed in an air current and should dry within half an hour or more quickly if warm air such as from a hair dryer is played upon it.

At the same time, because DuraFoam is buoyant, the patient can enter a therapeutic pool with the feeling of weightlessness and without the DuraFoam becoming soggy. A DuraFoam splint can even be made while the limb is immersed in warm water to obtain the maximum benefit from the relaxation and the warmth. As the moulding of a DuraFoam splint does not entail the use of water, it can be used in cold climates, where conventional plaster would freeze, thus rendering the material of doubtful value. This is of importance in military medicine, not only for first-aid measures, but for treating other conditions, such as fractures. Likewise, in the tropics dampness causes difficulty in storing as well as making water-using plasters.

Colours make the finished product very pleasing to the eye. This attractive appearance has a large part to play in the minds of the patients, their relatives and friends, to dissociate the old idea, engendered by the whiteness of the hospitals, of ill health and disability from the newer conception of convalescence, the recovery of function and the rehabilitation of the patient. Stewart,[3] in his empathy concept, has pointed out the importance of this morale-boosting and also the active identification with motivation towards a constructive goal.

DuraFoam is a very easy medium to use for the making of self-help devices. In a few minutes a knife, fork and spoon holder can be custom-made for the patient. A pen or pencil holder to fit around the hand with fingers twisted out of shape will make writing an easier task.

Apart from the patient, and the doctor himself, the people most likely to welcome this new medium are the physiotherapists and the occupational therapists. They are the most likely to work with it as they are longer and more practically in contact with the patient by the very nature of their work. They assess his capabilities and train his abilities, and are anxious to prevent any disability. Indeed this has been our experience with this material to date. These rehabilitation therapists have shown by their enthusiastic acceptance of this material that they are capable of developing it with new designs, both for supportive splints and self-help devices.[6]

I acknowledge with thanks the co-operation of Dura-Design Plastics Limited of Toronto, who supplied the DuraFoam kits for our clinical trials, and appreciate the encouragement of Mr. G. E. Parsons, whose grant and support made the work possible.

Lt.-Col. Harry F. Pierce, M.B.E., an Oxford graduate, the inventor, and Michael C. Nadas, chemical engineer and Toronto graduate, who formulated DuraFoam, were very helpful throughout the series, as was Walter G. Alley, M.Comm.(Tor.), who prepared the visual aids.

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2. SIMMONS, E. H. AND COX, L. A.: *Ibid.*, 76: 941, 1957.
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RÉSUMÉ

Il existe maintenant un nouveau matériau pour la confection d'appareils de contention pour fracture ou difformité orthopédique. Cette matière plastique (DuraFoam) en plus de posséder la rigidité du plâtre, est à la fois légère, imperméable à l'eau et translucide aux rayons X. Elle se présente sous forme d'une enveloppe plastique transparente qui s'applique directement à la peau, s'adapte au membre où siège la lésion, et dans laquelle on verse un mélange pâteux qui prend et durcit en quelques minutes. La facilité et la propreté de sa manipulation ne sont pas ses moindres avantages. L'appareil peut regagner sa malléabilité à la chaleur, ce qui permet en certaines circonstances de le refaçonner au lieu de le remplacer.

INTRACRANIAL CALCIFICATION FOLLOWING TUBERCULOUS MENINGITIS IN CHILDREN

Serial roentgenograms of the skull were taken in 130 cases of children who recovered from tuberculous meningitis two to ten years ago; 120 are alive at the time of the present report; 10 died 21 months to six years after the meningitis.

Pathologic intracranial calcification was detected during life in 63 children (48.4%); in two others, intracranial calcification and even ossification were found at necropsy. In most cases the calcification became detectable two to three years after the onset of the disease, but in some it was not detectable for five years.

Calcification was mainly seen: (1) in the basal meninges and (2) within the brain substance. The latter was the more common, and was seen in 49 cases (37%). The incidence of meningeal calcification progressively increased from 21% in patients in the early stage of the disease on admission to 55% in patients in the advanced stages. There was no appreciable difference in the incidence between those treated with streptomycin alone and with streptomycin-PAS, but the incidence of calcification was a little less in those treated with isoniazid-streptomycin. The use of intrathecal tuberculin and streptokinase also reduced the incidence of meningeal calcification.

Intracerebral calcification was seen in 17 children (13%). The incidence was independent of the stage of the disease on admission and of the method of treatment.

The incidence of calcification was higher among 21 children with neurologic sequelæ (62%) than in the others (46%), but the differences are not significant. Intracranial calcified lesions may harbour living tubercle bacilli. All six children who later relapsed had intracranial calcification.

Tuberculous meningitis is probably becoming the most common cause of intracranial calcifications in children.—J. Lorber: *Am. Rev. Tuberc.*, 78: 38, 1958.

THE SHEEP ERYTHROCYTE AGGLUTINATION TEST IN RHEUMATOID ARTHRITIS*

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DURING THE PAST DECADE, extensive work in many laboratories has clearly established the presence in the serum of most patients with rheumatoid arthritis of a protein, probably a macroglobulin,[1, 2] which is able to combine with the gamma globulin of a variety of animal species. This combination is best demonstrated by attaching the gamma globulin to some sort of carrier such as red cells or polystyrene latex particles, and then adding serum from a case of rheumatoid arthritis ("rheumatoid serum"). Union of its contained protein, designated as rheumatoid factor, with the gamma globulin, produces macroscopic agglutination of the carrier particles. Many systems have been based on this principle and have been recently reviewed by Ziff.[3]

Three tests are currently in common use. The F II test involves the binding of human pooled gamma globulin (Cohn Fraction II) to sheep cells by their preliminary treatment with tannic acid.[4] In the latex particle fixation test, polystyrene latex particles of uniform diameter serve as the inert carrier and are coated with human gamma globulin.[5] The procedure reported in this paper is a modification of the first method to be used extensively, namely the sensitized sheep erythrocyte agglutination test. It has undergone a number of modifications since its introduction by Waaler in 1940[6] and Rose *et al.* in 1948.[7]

The procedure in common use is to heat the sample of rheumatoid serum to be tested in order to inactivate complement, and then to absorb the serum with packed sheep cells in order to remove a heterophil antibody present in many human sera which will itself agglutinate sheep red cells. Then the euglobulin fraction of the serum is separated and mixed in serial dilution with sheep red cells that have been sensitized with a subagglutinating dose of rabbit antisheep cell serum. If rheumatoid factor is present in the serum, it reacts with the rabbit immune globulin coating the sheep cells, causing them to agglutinate. The use of euglobulin fraction rather than whole serum increases the sensitivity of the test by partial removal of inhibitors, and at the same time decreases the number of false positive reactions by eliminating certain agglutinating factors other than the factor or factors present in rheumatoid arthritis.[8]

*From the Departments of Bacteriology and Medicine, Queen's University. Supported by a grant from the Canadian Arthritis and Rheumatism Society.
Presented at the Annual Meeting of the Canadian Rheumatism Association, Vancouver, B.C., June 1958.

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Critics of this test have emphasized the difficulties in standardizing reagents, in reading the end point of the test, and in accurately reproducing results. This paper presents a method which overcomes these objections and is relatively easily performed and interpreted in a routine clinical laboratory; and it evaluates the usefulness of the test using data obtained over the past two years.

METHODS

Preparation of Test Sera

Euglobulin was rapidly precipitated from rheumatoid serum by dilution with 0.0027N hydrochloric acid after the method of Erickson *et al.*[9] The precipitate obtained was reconstituted to the original volume of serum in buffered saline at pH 7, then inactivated at 56° C. for ½ hour, and twice absorbed with an equal volume of packed sheep red cells for one hour at 37° C.

Preparation of Sensitized Sheep Erythrocytes

All titrations were performed in standard M.R.C. Perspex trays originally designed for hæmagglutination tests with influenza virus. These trays contain 10 rows of 8 smooth-bottomed cups each with a diameter of 1.5 cm. and a capacity slightly greater than 1 ml. The trays during incubation were covered with a sheet of glass cut to size. After use they were easily cleaned by a rinse in tap water, a soak in detergent and a final thorough rinse in tap water.

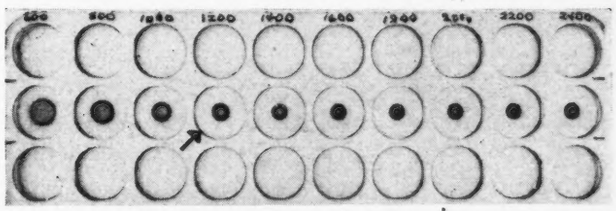

Fig. 1.—Amboceptor titration against sheep erythrocytes in cups of standard M.R.C. Perspex tray. An arrow marks the ideal dilution.

Sheep cells were collected in 250-ml. bottles containing 70 ml. of dextrose, sodium citrate (2.3 g. dextrose, 1.7 g. sodium citrate per 100 ml.), and the cells remained perfectly suitable for testing over periods of storage of up to one month. Each lot of antisheep cell rabbit serum or amboceptor must be titrated against each lot of sheep cells in order to determine the optimum sensitizing dose. Sheep cells were washed three times, diluted to a 1% suspension and mixed with equal volumes of serially diluted homologous amboceptor (1/600, 1/800, 1/1000, etc.), in test tubes and incubated for one hour at 37° C. Then 0.25 ml. of each suspension was added to 0.25 ml. of saline in the cups of the trays, incubated a further hour and placed at 5° C. overnight. The results of such a titration are indicated in Fig. 1.

The dilution of amboceptor used is that which makes the red cells settle into a doughnut pattern

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with the diameter of the hole equal to the width of the rim. This dilution of amboceptor was then incubated with an equal volume of 1% cell suspension at 37° C. for one hour. The resulting 0.5% suspension was generally used the same day it was prepared, but surprisingly enough most preparations were found to remain suitable for three or four days if stored at 5° C. No difference was found in controlled titrations using sensitized cells prepared only twice a week as opposed to those prepared daily.

The Agglutination Tests

Serial two-fold dilutions of euglobulin fraction were made in 0.25 ml. volumes of saline in the cups of the tray such that the starting dilution was 1 in 4. To each cup was added 0.25 ml. of the sensitized red cell suspension. The tray was then shaken gently to disperse the erythrocytes evenly, covered with a glass plate, and incubated first at 37° C. for one hour and then at 5° C. overnight, and the agglutination end point was read by the pattern of the cells as illustrated in Fig. 2. Unsensitized

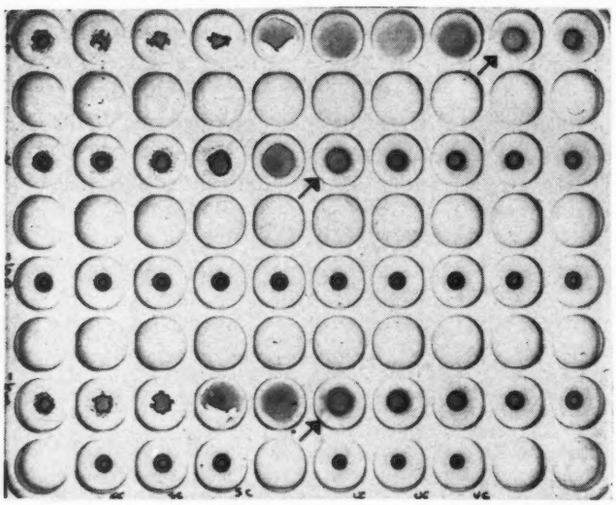

Fig. 2.—Serial dilutions of euglobulin fraction from 1:8 to 1:4000 mixed with sensitized sheep cells in perspex cups in rows 1, 3, 5 and 7. Positive agglutination reactions in rows 1, 3 and 7, with end points indicated by arrows. Negative agglutination reaction in row 5. Control sensitized cells in row 8 on left. Control unsensitized cells in row 8 on right.

cells settle in a compact button at the bottom of the cup. Sensitized cells settle into the doughnut pattern previously described. The first sign of agglutination is an increase in the size of the hole in the doughnut. As agglutination becomes more complete, the hole increases in diameter and the rim of the doughnut disappears until the cells form a thin layer covering the entire bottom of the cup. When agglutination is very strong, the edges of this sheet of cells curl and crinkle. The most satisfactory end point was found to be a pattern of cells still showing a definite peripheral ring, but with a diameter about half that of the cup. The titre is expressed as a reciprocal of the final dilution of euglobulin associated with this pattern.

RESULTS AND DISCUSSION

Tests have now been completed on one or several occasions on sera of 294 patients—86 with rheumatoid arthritis, 104 with other rheumatic diseases, and 104 who served as controls. The data are presented in Table I.

Positive sheep cell agglutination reactions were recorded in 75 out of 86 cases of rheumatoid arthritis (over 85%), and 50% had titres of 256 or higher. These results are in marked contrast to the findings in other rheumatic diseases where only 23 of 104 cases (less than 25%) registered positive titres, and only 4 cases (less than 5%) were positive in a dilution of 256 or greater. The control cases, 104 in all, were with one exception negative. The single exception was a weakly positive reaction in the first dilution. Controls were composed of healthy medical students and hospital patients with miscellaneous but no rheumatic diseases.

All 86 cases of rheumatoid arthritis in this series would be classified, according to the diagnostic criteria proposed by the American Rheumatism Association, as definite rheumatoid arthritis; that is to say, articular and periarticular aching and stiffness had been present for a period of at least six weeks, and was accompanied by demonstrable swelling in at least two peripheral joints. The 11 cases with negative agglutination reactions are worthy of special comment. Three of them had what appeared to be rheumatoid arthritis—polyarticular inflammation and high sedimentation rates—but in each case the disease was less than six months in duration. Two other patients who had suffered from mild rheumatoid arthritis were in remission when sheep cell agglutination was tried and found negative. One interesting patient was followed up for many years with a polyarticular arthritis, leukocytosis and eosinophilia, and associated bronchitis and emphysema. The clinical diagnosis wavered between rheumatoid arthritis and polyarteritis nodosa. His sheep cell agglutination reaction was negative. A small boy of five with rheumatoid arthritis had a negative test. His arthritis began acutely at the age of 22 months, pursued a severe and disabling course, and was accompanied by a moderate anæmia, a high sedimentation rate and grossly disturbed serum protein fractions. Most interesting of all were four adult patients with classical rheumatoid arthritis of moderate severity and duration, but with negative agglutination reactions. One woman's disease was of five years' duration. It had begun rather acutely and for the first few months of its course was accompanied by moderate fever. As time went on, various joints had become inflamed and a good deal of absorption of the articular ends of the bones took place. No nodules had formed. A second patient had suffered an equally acute onset to her disease, and over a two-year period had developed marked destructive changes in a number

TABLE I.—SENSITIZED SHEEP CELL AGGLUTINATION TITRES IN RHEUMATOID ARTHRITIS, OTHER RHEUMATIC DISEASES AND CONTROLS

Group	*Cases*	*Positive*	*Titre*											
			8	*16*	*32*	*64*	*128*	*256*	*512*	*1M*	*2M*	*4M*	*8M*	*16M*
Rheumatoid arthritis...	86	75 (87.2%)	3	4	8	9	8	8	9	9	10	5	1	1
Other rheumatic diseases	104	23 (22.1%)	9	8	1	—	1	2	1	1	—	—	—	—
Controls.....	104	1 (0.9%)	1	—	—	—	—	—	—	—	—	—	—	—

of her joints. So much ankylosis had developed, in fact, that an infective type of arthritis was suspected, but never proven. Iritis kept recurring but no nodules formed. The third case is now of nine years' duration and displays a moderate degree of multiple joint damage. The last case is of only 18 months' duration and has been featured by a good deal of joint inflammation but little joint destruction. An unusual component has been the association of some soft tissue thickening in the hands similar to that seen in the shoulder-hand syndrome, but the generalized joint reaction, the anæmia, the elevated sedimentation rate and the osteoporosis, all indicate the presence of rheumatoid arthritis.

The incidence of over 85% positive agglutination tests in this series is comparable to the experience of others using a similar technique.[8, 10-14] Of course, the exact percentage of positive tests in any series depends upon both case selection and laboratory procedure. Because the test is so often positive in rheumatoid arthritis and despite the fact that false positive reactions occur in other rheumatic diseases, particularly in the collagen group, it has become widely adopted as a diagnostic test without as yet any clear understanding of its significance. So far no obvious correlation has been demonstrated between the strength of the agglutination reaction and any clinical or laboratory feature of rheumatoid arthritis, but such a correlation poses problems because of the difficulty in singling out discrete components of rheumatoid disease. It is generally agreed that rheumatoid sera are more likely to cause agglutination after the disease is well established, with joint destruction and nodule formation as a part of the clinical picture, but there is less agreement on the significance of disease activity, no doubt in part because of the difficulty in defining activity. When the inflammatory reaction in rheumatoid disease is reversed with steroid therapy, the titre apparently does not change.[2, 15]

The prognostic significance of high or low titres and of changing titres is not as yet established, and one of the reasons for this has been the difficulty in accurately reproducing titres in any given patient. A number of the cases in this series have been tested on repeated occasions over periods as long as 40 weeks. The longer the lapse in time between tests the greater the degree of variability in the titre, as shown in Table II. It should be noted that this table does not record the distribution of changes in a single group of patients followed throughout a period of 40 weeks, but rather the results on 38 different subjects tested at various intervals. These variations in titre have been shown to be independent of technical variation. Four batches of positive sera were stored, and over a 10-20 week period some 36 tests were carried out with different batches of amboceptor and red cells of various ages. Identical results were recorded in 34 and only one tube dilution difference in the other two.

It is thus clear that significant changes in titre have been observed and these undoubtedly reflect some change in the disease process. Work is now progressing to determine what correlation exists between these changes, the course of the disease, and the effect of therapy.

OTHER RHEUMATIC DISEASES

There were a number of positive agglutination tests in other rheumatic diseases (23/104) but the highest incidence of these (11/25), and all five of the high titres, were found in other collagen diseases which overlap rheumatoid arthritis in their clinical and pathological features (Table III). It has been suggested that some of these positive reactions may be due to the presence of an agglutinating factor, other than the rheumatoid factor, which is detected but cannot be distinguished by the test systems currently in use.

TABLE II.—CHANGE IN TITRE OF POSITIVE CASES FOLLOWED UP FOR VARIOUS PERIODS OF TIME

Time after initial test	*Total tested*	*Arbitrary titre (2 × dils.)*								
		−4	*−3*	*−2*	*−1*	*0*	*+1*	*+2*	*+3*	*+4*
1 week.....	23	—	—	—	—	21	2	—	—	—
2- 7 weeks.....	21	—	—	1	5	8	5	2	—	—
8-16 weeks.....	21	1	—	1	3	4	11	1	—	—
17-40 weeks.....	24	—	1	2	3	5	5	4	3	1
Initial euglobulin fraction lyophilized 10-20 weeks.....	36	—	—	—	1	34	1	—	—	—

TABLE III.—SENSITIZED SHEEP CELL TITRES IN MISCELLANEOUS RHEUMATIC DISEASES

Group	No. of cases	Positive	Titre 8	16	32	64	128	256	512	1M	2M	4M	8M	16M
Collagen diseases	25	11												
Arthritis with psoriasis	3	0	—	—	—	—	—	—	—	—	—	—	—	—
Ankylosing spondylitis	12	5												
—with peripheral joint involvement	3	2	—	1	—	—	—	—	1	—	—	—	—	—
—without peripheral joint involvement	9	3	—	1	—	—	—	2	—	—	—	—	—	—
Acute rheumatic fever	5	2	1	—	—	—	1	—	—	—	—	—	—	—
Disseminated lupus erythematosus	1	1	—	—	1	—	—	—	—	—	—	—	—	—
Polyarteritis nodosa	2	2	1	—	—	—	—	—	1	—	—	—	—	—
Erythema nodosum	2	1	—	1	—	—	—	—	—	—	—	—	—	—
Degenerative joint disease	52	6	3	3	—	—	—	—	—	—	—	—	—	—
Fibrosis, periarthritis, psychosomatic rheumatism	18	6	4	2	—	—	—	—	—	—	—	—	—	—
Gout	6	0	—	—	—	—	—	—	—	—	—	—	—	—
Infective arthritis	3	0	—	—	—	—	—	—	—	—	—	—	—	—

This series of miscellaneous rheumatic diseases is small but certain findings deserve comment. Three cases of psoriasis and arthritis were negative, one patient being an elderly man with severe joint disease who eventually died. Negative results with this combination of diseases are the rule and suggest something different about the disease mechanism from that in uncomplicated rheumatoid arthritis. No data have been obtained so far to justify splitting cases into a group called psoriatic arthritis and another called rheumatoid arthritis with psoriasis. Five of 12 cases with ankylosing spondylitis were positive, 3 with high titres. There is some indication that cases with associated peripheral joint involvement are more apt to be positive than those without, but their disease is generally more severe.

The finding of 6 weakly positive titres in 52 cases of degenerative arthritis is perhaps not surprising, since clinical differentiation between arthritis which is purely degenerative and that which is purely rheumatoid is sometimes difficult. Many patients display a picture of predominantly focal degenerative joint disease which is accompanied by a more generalized aching and stiffness and slight elevation of sedimentation rate. This is particularly apt to be the case in women at the time of the menopause when Heberden node formation occurs at the terminal interphalangeal joints.

Six of 18 patients with fibrositic syndromes, variously labelled as fibrositis, periarthritis, psychosomatic rheumatism, etc., have had positive tests. This group, composed of tense, anxious patients with diffuse aching and stiffness in and around their joints with little to find on clinical examination, and sometimes with a mild to moderate elevation of sedimentation rate, are among the most difficult rheumatic problems to assess. The criteria for diagnosis of rheumatoid arthritis proposed by the American Rheumatism Association are so loose that many of these cases would qualify as probable or possible cases of rheumatoid arthritis. However, when first seen, it may be a matter of some difficulty to separate those patients who suffer simply from psychosomatic rheumatism from those who later on develop classical rheumatoid arthritis or some other type of collagen disease. It is possible that the sheep cell agglutination test may have its most useful clinical application sorting out this type of problem case. Hall *et al.* have recently reported 11 such cases with positive latex reactions who have subsequently developed definite rheumatoid arthritis.[16]

The few cases of gout and infective arthritis in this series were uniformly negative.

CONCLUSION

A technique for carrying out the sensitized sheep agglutination test which is relatively easily performed in a routine clinical laboratory, has an easily read end point, and is reproducible, has been described.

Experience obtained with the test in cases of rheumatoid arthritis and other rheumatic diseases has been presented and the significance of the results discussed.

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RÉSUMÉ

Le sérum de la plupart des malades atteints de polyarthrite chronique évolutive contient une protéine qui possède la propriété de se combiner à une globuline gamma de certaines variétés animales. Cette protéine (qui serait une macroglobuline) est à la base des épreuves d'érythrocyte de mouton ou de particules de latex. Les auteurs de cet article décrivent une modification de la technique du test F II, la préparation des réactifs et les critères dans l'interprétation des résultats. Une série de 294 sujets furent soumis à cette épreuve, à savoir 86 malades atteints de la polyarthrite chronique évolutive, 104 malades atteints d'une

autre forme quelconque d'arthrite et 104 témoins. Parmi les victimes de la maladie de Charcot on obtint 87.2% de résultats positifs dont plusieurs l'étaient à une dilution très élevée. Dans les autres formes d'arthrite, les résultats positifs s'élevèrent à 22.1%, alors que seulement 0.9% des témoins normaux ou non arthritiques fut positif. Les 11 cas de polyarthrite chronique évolutive qui donnèrent des résultats négatifs se répartissent comme suit: trois d'entre eux étaient malades depuis moins de six mois, deux ne portaient que des atteintes légères et étaient en état de rémission, un autre était un cas douteux présentant certains aspects de la polyartérite noueuse, un autre était un petit enfant de cinq ans et enfin, les quatre derniers étaient des adultes qui offraient le tableau clinique classique de la P.C.E. Il est intéressant de noter que les résultats positifs obtenus chez les malades atteints d'autres formes d'arthrite le furent le plus souvent dans des cas de maladies du collagène qui semblent posséder certains faits en commun avec la polyarthrite. Il est à remarquer que les cas de goutte et d'arthrite infectieuse furent négatifs. La valeur pronostique de cette épreuve n'est pas encore établie. On sait que l'amélioration produite par les stéroïdes ne semble pas affecter les résultats du test, mais jusqu'à présent il a été très difficile d'interpréter les variations considérables que l'on observe dans les différents titres chez le même malade au cours de l'évolution de sa maladie.

THE EXPERIMENTAL PRODUCTION OF ATHEROSCLEROSIS IN SWINE FOLLOWING THE FEEDING OF BUTTER AND MARGARINE

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THERE IS EVIDENCE which indicates that fibrin deposits are a factor in the etiology of atherosclerosis.[1, 2] Patients with clinical manifestations of atherosclerosis have more active clotting systems than controls.[3, 4] It is not unreasonable to speculate that the increased activity of the clotting mechanism in atherosclerotic individuals is a factor in fibrin deposition and the pathogenesis of atherosclerosis. The activity of the clotting system is determined to some extent by the type of fat in the diet. Butter accelerates clotting both *in vitro* and *in vivo*, while margarine has little activity.[5, 6] Therefore, if the activity of the clotting system is, as this evidence suggests, a factor in the development of atherosclerosis, feeding animals a coagulant active fat (butter) could be expected to produce more atherosclerosis than the feeding of relatively inactive fat (margarine). The following experiment was done to test this hypothesis.

Thirty-three swine matched for age, sex, weight, breed and nature of their coagulation mechanism were divided into three groups. Pigs in group A were fed butter to 40% of their calories and a commercial hog grower ration; those in group B were fed margarine to 40% of their calories and hog grower; and those in group C were fed grower ration only. After three to nine months on this regimen the swine were killed and examined. The following investigations were carried out: blood lipids, nature of the coagulation mechanism, and the gross and microscopic examination of the vessels and organs.

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It was decided to use swine in this study because the cardiovascular system of the pig resembles that of the human, and pigs develop a form of spontaneous atherosclerosis. The omnivorous nature of the pig allows him to adjust readily to a high fat diet. The size of the pig permitted large quantities of blood to be easily obtained for test purposes.

MATERIALS AND METHODS

Swine.—The pigs used were of the Yorkshire breed or Landrace-Yorkshire cross breeds obtained from two separate sources. At the beginning of the experiment the swine were three to four months of age with an average weight of approximately 125 lb.

Feeding.—Each group of 11 pigs was housed in a hut with access to a small paddock. The swine were fed in individual feeding pens so constructed that they remained in the pens until the food was consumed. The control pigs had access to their feed from a self-feeder. Adequate water supply was provided in all pens. The fat-enriched diets were made by adding a measured amount of melted butter or margarine* to a measured amount of hog grower. The pigs receiving fat were started on a diet containing 20% of the calories as fat. During a period of four weeks the fat was increased to 40% of the diet. The diets for the butter and margarine fed animals were isocaloric. The grower ration contained 15% crude protein, 2% crude fat, and 8% crude fibrin.†

Blood samples.—Samples were secured from the anterior vena cava by the method described by Hoerlein.[7] Paraffinized 20 ml. glass syringes with 18 gauge 2"-3½" silicone-coated stainless steel needles were used. Venipunctures contaminated with tissue juices were discarded, and the venipuncture was repeated. The pigs were anæsthetized when blood samples were taken. The animals were restrained and ether was administered until relaxation occurred. Intra-

*The brand of margarine used was inactive in clotting.
†The ingredients listed in the commercial grower were: vitamin B_{12} supplement, riboflavin supplement, "D" activated plant sterol, vitamin A feeding oil, meat scrap, condensed fish solubles, fish meal, soybean oil meal, molasses, dehydrated alfalfa meal, ground barley, ground oats, ground No. 1 feed screenings, wheat shorts and/or middlings, ground limestone, defluorinated phosphate, manganese sulphate, cobalt carbonate, copper oxide, zinc oxide, 0.5% iodized salt, chlortetracycline hydrochloride. The total tocopherol content of the grower ration as determined by the Department of Nutrition at the Ontario Agricultural College was 4.6 mg. per 100 g. of feed.

venous pentobarbital sodium* was then given until the proper effect was obtained.

Blood pressure.—At the completion of each study the blood pressure was obtained by exposing the external carotid and ligating the vessel distally. A polyethylene tube was inserted, tied in place and connected to a Sanborn electromanometer. The pressures were recorded on a Poly-viso recorder along with the electrocardiogram.

Lipid studies.—The cholesterol levels were determined by a modified Sperry Schonheimer technique.[8] The phospholipids were determined by the technique of Zilversmit and Davis.[9]

Coagulation studies.—These were carried out during the fasting state using techniques previously described.[10] The $Al(OH)_3$-treated plasma used in the thromboplastin generation test at the completion of the study was diluted 1:10 with 0.85% saline instead of 1.5. The initial tests at the start of the study were carried out using swine $Al(OH)_3$-treated plasma diluted 1:5.

Termination of study.—The pigs were destroyed by exsanguination.

Gross and Microscopic Examination of Vessels and Organs

Gross.—Aorta, carotid, renal and coronary arteries were examined and graded in the following manner:

Size of lesion (greatest dimension)	*Grade*	*Number*	*Grade*
(A) 1 - 2 mm.	1/8	3 - 5	1/4
		5 - 10	1/2
		10 - 20	3/4
		20 -	
(B) 3 - 5 mm.	1/4	Same as for A.	
(C) 5 - 10 mm.	1/2	2 - 5	1/2
		5 - 10	3/4
		10 -	1
(D) 1 - 2 cm.	3/4	Same as for C.	
(E) 2 cm.	1	2 - 5	1/2
		5 -	1

Microscopic examination.—Sections of the cardiovascular system were fixed in buffered formol calcium solutions. Sections were taken through areas of obvious gross lesions and at vessel bifurcations where there was no evidence of gross lesions.

Sections were stained by the following methods: hæmatoxylin and eosin; periodic acid-Schiff test for glycolipids; lipid stains; oil red "O", Nile blue, acid hæmatin; Hales' stain for acid mucopolysaccharides; thionin and toluidine blue for metachromasia; Verhoeff's Van Gieson for elastic membranes; Van Kossa for calcium; polarized light for cholesterol crystals; extractions with solvents for characterization of lipid.

RESULTS

Gross and Microscopic Examination of Vessels

Gross.—The total grade of atherosclerosis for group A (butter) was 30 1/8, group B (margarine) 11 3/8, and group C (no fat) 8 7/8. The mean grade for each group at the intervals during the study when the animals were killed is shown in Table I. The grade for group A was always greater than that for groups B and C. As the length of time the animals were fed increased, the mean grade in each group also increased. The swine killed after three months of feeding had the greatest number of plaques around the aortic valve and the ascending arch of the thoracic aorta. In animals killed at later periods, the disease was more marked in the abdominal aorta, especially around the area of bifurcation of the iliac vessels and the origin of the renal and mesenteric arteries (Figs. 1 and 2).

TABLE I.—GRADE OF ATHEROSCLEROSIS FOR EACH GROUP AT INTERVALS DURING STUDY

Period of feeding	*No. of swine killed in each group*	*Mean grade of atherosclerosis*		
		Group A	*Group B*	*Group C*
3 months	3	1 3/8	1/8	1/8
4 months	2	1	1/8	1/16
6 months	3	3 3/4	1 1/2	1 1/4
8 - 9 months	3	4 1/8	1 5/8	1 1/2

TABLE II.—THE DEGREE OF ATHEROSCLEROSIS AT THE CAROTID BIFURCATION IN EACH GROUP

	Group A	*Group B*	*Group C*
No. of swine with involvement of either carotid bifurcation	8	3	3
Right carotid bifurcation involved	7	3	2
Left carotid bifurcation involved	5	0	1
Total grade of atherosclerosis both carotid bifurcations	4 7/8	3/4	1 1/8

Plaques were found at the bifurcation of the carotid vessels in animals killed after the first three months of feeding. All eight butter-fed animals killed in this period had plaques at the carotid bifurcation, whereas only three of eight margarine-fed and three of eight control animals had plaques (Table II). Butter-fed swine killed during the final eight to nine months of the study showed small atheroma in the renal vessels at

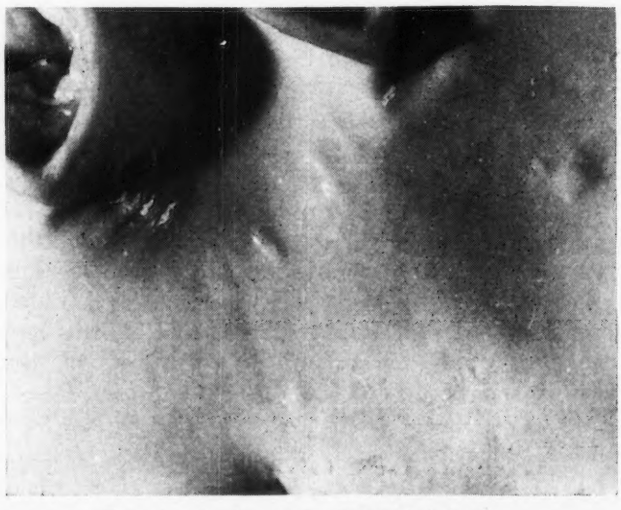

Fig. 1.—Aortic arch, butter-fed swine.

*Nembutal—Abbott Laboratories, Montreal.

Fig. 2.—Abdominal aorta, bifurcation of iliac arteries, butter-fed swine.

points of bifurcation and in the coronary vessels. The last pig destroyed in the control group had a patent ductus arteriosus. This was the only congenital vessel abnormality observed throughout the study. There was considerable atheroma in the aortic arch, particularly around the patent ductus. This pig accounted for the highest grade in the control group.

Microscopic examination.—The plaques were intimal thickenings composed of varying amounts of connective tissue, hyaline material and a cellular infiltrate of macrophages and lymphocytes (Fig. 3). In some instances the internal elastic lamina was broken with extension into the media (Fig. 4).

Stains for sudanophilic material showed fine droplets of fat next to the internal elastic lamina or subendothelial in most plaques of the butter-fed group (Figs. 5 and 6). Sudanophilic droplets were present in some atheroma in the pigs fed the non-fat diet. The special stains for various lipids indicated that neutral or non-acidic fats made up most of the sudanophilic material, and phospholipids were present. Cholesterol crystals were found in some plaques examined using the polarizing microscope. The Von Kossa technique failed to reveal any evidence of calcification. In some plaques, especially well-established aortic atheroma, there was evidence suggestive of vascularization (Fig. 7). Metachromasia and acid mucopolysac-

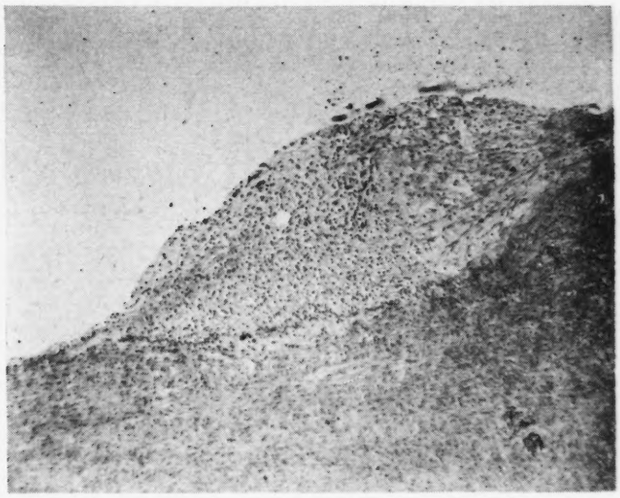

Fig. 3.—Section through an aortic plaque. H. and E. × 75.

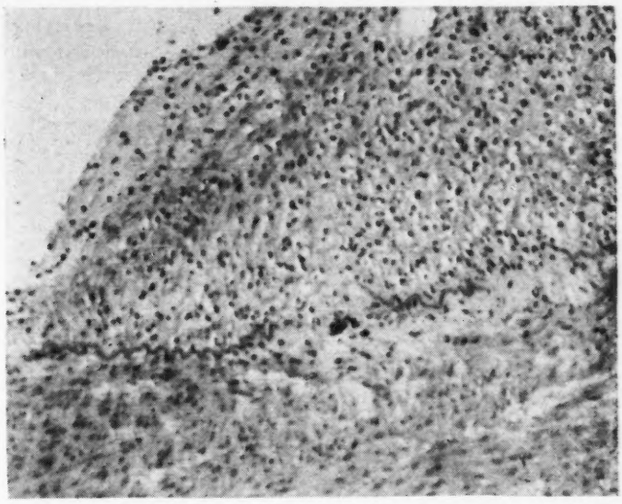

Fig. 4.—Enlargement of area in Fig. 3, showing disrupted elastic lamina. H. and E. × 150.

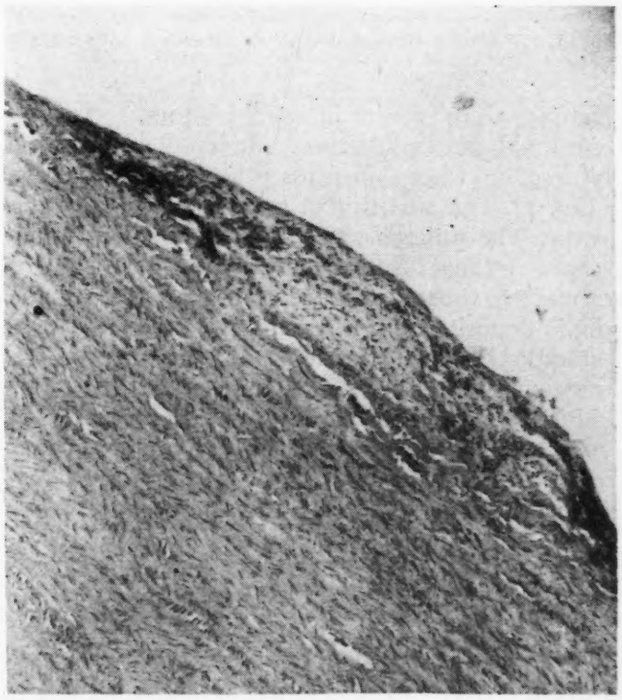

Fig. 5.—Section through aortic plaque stained with Oil red "O". Dense dark areas represent sudanophilic material. × 100.

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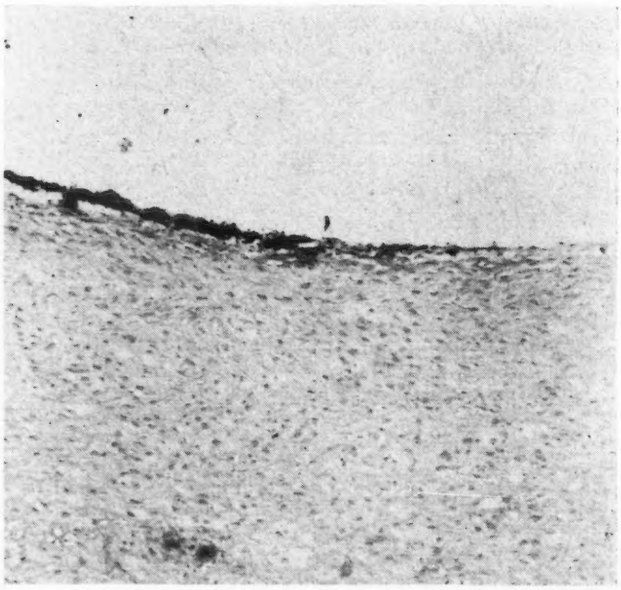

Fig. 6.—Section through margin of a plaque stained with Oil red "O" showing fat deposits below endothelium. × 100.

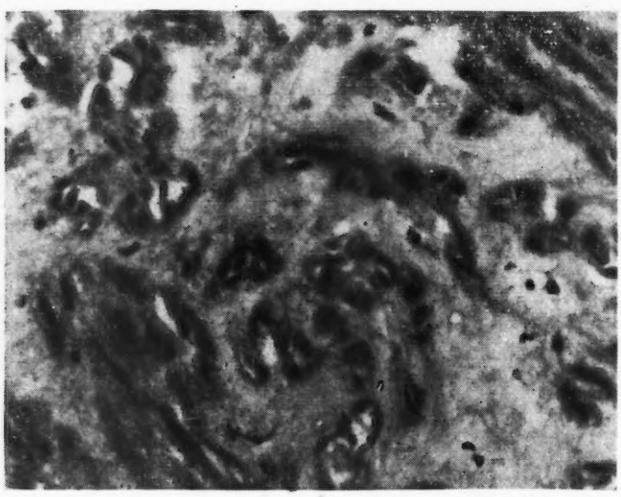

Fig. 7.—Section through an aortic atheroma showing suggestive evidence of vascularization. H. and E. × 500.

charides were present in many plaques.

Intimal thickening was observed at areas of bifurcation where no gross atheroma was present (Fig. 8). This was true of both fat and non-fat fed swine. The pulmonary artery had areas of microscopic intimal thickenings which consisted of connective tissue and loose hyaline masses. Sudanophilic deposits were found in these deposits. Such alterations were prominent at the edge of the ductus arteriosus scar in all animals.

Blood pressures and electrocardiograms.—There were no significant differences between blood pressures and heart rates of the pigs fed different diets. Electrocardiograms indicated that there were no cardiac irregularities.

TABLE III.—WEIGHT OF ANIMALS DURING THE STUDY

Length of time on feeding experiment	*Number of animals*	*Mean weight of animals at completion of each period of study—pounds*		
		Group A	*Group B*	*Group C*
3 months	3	252	264	289
4 months	2	275	244	323
6 months	3	391	385	389
8 - 9 months	3	423	450	433

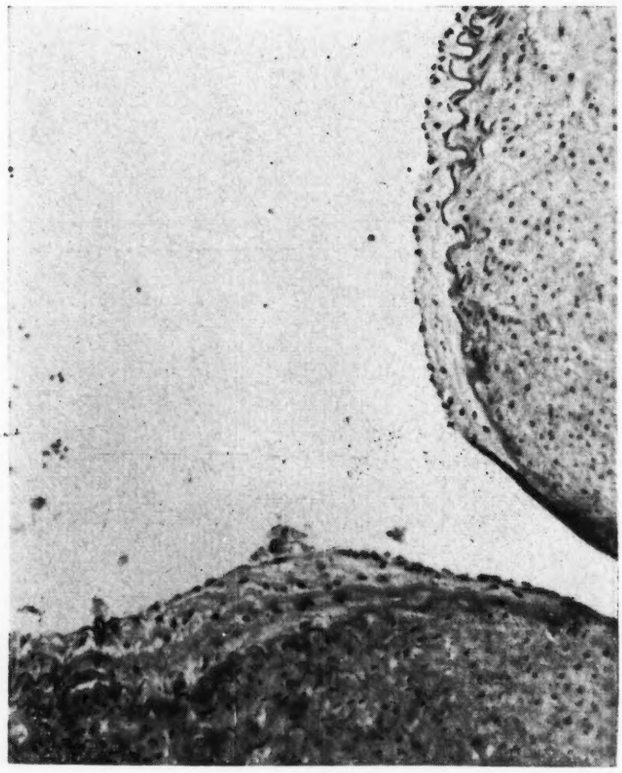

Fig. 8.—Section from bifurcation of carotid artery. No gross evidence of plaque formation. H. and E. × 200.

Weight.—The mean weights for the animals killed at each period of this study were similar (Table III). All animals gained weight during the study.

Lipid.—There was no elevation of the blood cholesterol and phospholipid in the fat-fed swine at the completion of the study (Table IV). Furthermore, there was no increase of these lipid levels in the butter-fed swine with the most atherosclerosis (Table V).

Blood coagulation.—The mean fasting coagulation values for each group showed no definite difference at the start of the experiment. The fasting coagulation indices at the completion of the study showed some differences. The mean platelet count was highest in the butter-fed group and least in the animals receiving no fat (Table VI). The difference between the mean values for these two groups was statistically significant. There were no definite differences between the Russell viper venom times, as shown in Table VI. The plasma activity (Table VII) in the thromboplastin generation test was greatest for the butter-fed swine and least for the margarine-fed and non-fat-fed animals. The differences between the mean values were not significant on a statistical basis. Although the differences were less marked, there was a tendency for the $Al(OH)_3$-treated plasma from the butter-fed animals to be more active in the thromboplastin generation test (Table VIII). The serum activity showed little difference (Table IX).

TABLE IV.—BLOOD LIPID VALUES FOR THE SWINE AT THE START AND END OF STUDY

	Group A		*Group B*		*Group C*	
	Start	*End*	*Start*	*End*	*Start*	*End*
Cholesterol mg.%						
Total—Mean	89.5	87.1	91.0	85.7	115.1	92.1
S.D. ±	18.1	12.9	9.0	13.2	22.8	16.1
S.E.	5.94	4.10	2.84	4.17	8.06	5.10
Free—Mean	19.4	18.1	20.6	20.0	35.3	21.1
S.D. ±	4.8	2.5	3.2	5.7	4.6	7.3
S.E.	1.53	0.80	1.01	1.8	1.64	2.32
Ester—Mean	70.1	69.0	70.4	65.7	79.8	71.0
S.D. ±	8.0	12.2	8.0	15.0	21.6	14.6
S.E.	2.54	3.87	2.54	4.8	7.64	4.61
Phospholipid mg.%						
Mean	123.2	93.8	95.4	85.2	129.5	83.9
S.D. ±	22.1	25.1	24.5	16.8	29.0	16.2
S.E.	6.09	7.93	7.76	5.3	10.25	5.13
C/P ratio						
Mean	0.730	0.956	1.004	1.025	0.897	1.126
S.D. ±	0.128	0.288	0.241	0.214	0.130	0.218
S.E.	0.041	0.093	0.078	0.068	0.042	0.069

S.D. = Standard deviation.
S.E. = Standard error.

TABLE V.—CHOLESTEROL AND PHOSPHOLIPID VALUES FOR BUTTER-FED SWINE WITH THE MOST AND LEAST ATHEROSCLEROSIS AT THE BEGINNING AND COMPLETION OF THE FEEDING EXPERIMENT

	Swine with the most atherosclerosis (5)		*Swine with the least atherosclerosis (6)*	
	Start	*End*	*Start*	*End*
Cholesterol mg.%				
Total—Mean	96.8	81.8	83.5	91.5
S.D. ±	6.8	5.6	4.8	16.0
S.E.	3.03	2.53	1.92	6.8
Free—Mean	21.9	17.4	17.8	19.0
S.D. ±	4.6	2.8	4.8	2.2
S.E.	2.04	1.24	1.92	0.88
Ester—Mean	74.9	64.3	65.7	72.4
S.D. ±	8.1	5.6	11.6	15.2
S.E.	3.6	2.50	4.65	6.10
Phospholipid mg. %				
Mean	130.4	80.6	117.1	101.6
S.D. ±	19.2	4.9	24.0	22.8
S.E.	8.51	2.17	9.6	9.2

TABLE VI.—PLATELET COUNTS AND RUSSELL VIPER VENOM TIME FOR THE SWINE AT THE START AND END OF THE FEEDING EXPERIMENT

		Russell viper venom time sec.		*Platelet count No./c.mm. ×1000*	
Group		*Start*	*End*	*Start*	*End*
A Butter	Mean	13.8	16.5	423.0	317.0
	S.D. ±	4.0	4.1	88.0	94.0
	S.E.	1.28	1.31	26.6	28.4
B (Margarine)	Mean	13.4	16.3	412.0	292.0
	S.D. ±	4.1	4.0	90.0	62.0
	S.E.	1.3	1.28	27.2	18.7
C (No fat)	Mean	13.7	17.1	436.0	238.0
	S.D. ±	3.8	3.7	73.0	65.0
	S.E.	1.22	1.19	22.0	19.6

Probability of the difference between the mean values using the T test:
—All but the platelet counts for A and C at the end of the study >0.05.
—Difference between the mean platelet counts for A and B at the end of the study 0.05.

TABLE VII.—ACTIVITY IN THE THROMBOPLASTIN GENERATION TEST OF PLASMA (CHRISTMAS FACTOR) PREPARED FROM SWINE AT THE COMPLETION OF THE STUDY

	Incubation time in minutes				
Group	*1*	*2*	*3*	*4*	*5*
	Clotting time in seconds				
A (Butter)					
Mean	20.8	15.2	15.9	18.2	18.6
S.D. ±	24.3	8.2	6.6	5.4	11.0
S.E.	7.32	2.48	2.0	1.64	3.32
B (Margarine)					
Mean	22.5	17.3	19.9	22.6	25.3
S.D. ±	11.1	4.5	6.6	8.4	9.0
S.E.	3.40	1.36	1.99	2.54	2.70
C (No fat)					
Mean	24.3	20.4	18.4	20.2	22.4
S.D. ±	18.1	8.6	6.3	6.9	9.2
S.E.	5.45	2.60	1.90	2.08	2.78

The difference between the mean values was not found to be statistically significant using the T test.

TABLE VIII.—ACTIVITY OF $Al(OH)_3$-TREATED PLASMA PREPARED FROM THE SWINE AT THE COMPLETION OF THE STUDY IN THE THROMBOPLASTIN GENERATION TEST

	Incubation time in minutes				
Group	*1*	*2*	*3*	*4*	*5*
	Clotting time in seconds				
A (Butter)					
Mean	17.4	12.6	11.4	11.5	12.5
S.D. ±	21.0	19.2	8.2	9.2	9.6
S.E.	6.4	5.8	2.5	2.7	2.9
B (Margarine)					
Mean	19.2	13.3	12.3	13.6	14.4
S.D. ±	14.9	11.9	9.3	10.4	11.2
S.E.	4.50	3.60	2.80	3.15	3.37
C (No fat)					
Mean	15.4	12.2	11.9	13.1	14.0
S.D. ±	13.8	11.9	9.7	11.8	10.2
S.E.	4.17	3.60	2.93	3.56	3.08

The difference between the mean values was not found to be statistically significant using the T test.

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TABLE IX.—ACTIVITY IN THE THROMBOPLASTIN GENERATION TEST OF SERUM PREPARED FROM SWINE AT THE COMPLETION OF THE STUDY

Group	*Incubation time in minutes*				
	1	*2*	*3*	*4*	*5*
	Clotting time in seconds				
A (Butter)					
Mean	13.2	14.4	16.2	18.1	20.1
S.D. ±	3.1	3.2	6.1	6.2	7.5
S.E.	0.94	0.96	1.84	1.87	2.26
B (Margarine)					
Mean	12.6	13.3	14.2	16.4	18.1
S.D. ±	1.7	1.4	3.2	4.1	5.1
S.E.	0.51	0.42	0.96	1.24	1.54
C (No fat)					
Mean	15.3	13.0	15.3	16.0	20.4
S.D. ±	4.2	2.2	3.2	4.2	8.2
S.E.	1.25	0.66	0.96	1.25	2.5

The difference between the mean values was not found to be statistically significant using the T test.

If the coagulation indices for the butter group are divided on the basis of the animals with the most and least atherosclerosis at the completion of each feeding interval, there are more distinct differences. The five animals with the most atherosclerosis had the highest mean platelet count, and the greatest mean activity of serum, plasma and $Al(OH)_3$-treated plasma in the thromboplastin generation test (Table X). The differences between the mean values of some of the clotting indices for these animals and the margarine and non-fat fed animals were significantly different (Table XI).

DISCUSSION

Type of Fat and Vascular Disease

This study shows that swine develop some atherosclerosis on a low fat diet. Others have reported similar findings.[11, 12] Increasing the fat content of the diet by adding margarine to the feed did not lead to much increase in the amount of vascular disease, but the addition of butter to the diet did produce a greater incidence of lesions in the vessels. This indicates that the type of dietary fat is more important than the amount of fat in producing vascular disease in swine. There is considerable evidence that the type of fat is more important than the amount of fat in causing elevation of the blood lipids in humans and experimental animals.[13, 14] A recent investigation[15] showed that whereas a diet rich in butter elevated the blood lipids in Rhesus monkeys, a margarine-rich diet produced no change.

Blood Lipids

Bragdon[12] found that swine on a diet in which 40% of the calories were derived from butter had elevated cholesterol levels. The failure to produce a change in blood lipids in the present experiment is difficult to explain. Possibly the animals were not absorbing the fat adequately. However, the swine were given a fat-rich meal five to six hours before death, and post-mortem examination showed that the lacteals and lymphatic channels from the intestine were injected with fat. Furthermore, the animals gained weight in a uniform manner. Although indirect, this evidence indicates that the swine absorbed the fat. The failure to find a rise in the serum lipids may have been due to a factor in the hog grower ration.

Preliminary studies indicate that cooking the hog grower destroys a factor which prevents elevation of blood lipids in swine on high fat diets. Other reports indicate that factors such as vitamins and the quantity and quality of proteins in the diets are important in determining the lipid change and amount of disease in experimental atherosclerosis.[16, 18]

Nature of the Atheroma

The gross nature of the lesions and the pattern of evolution of the disease was similar to that described for humans by Duff and McMillan.[19] The microscopic characteristics of the plaques were also similar to that found in human atheroma. The disease in swine was more cellular and lacked the foamy appearance of the plaques found in rabbit atherosclerosis. The fact that lipid was present in some lesions of the control animals indicates that a high fat diet is not necessary for lipid deposits. The increased lipid deposits in the butter-fed group shows that the addition of certain types of fat to the diet increases the amount of lipid found in the atheroma. However, it is not necessary for the blood lipids to be elevated in swine for this to occur. This could mean that fat imbibition was not the main factor in the etiology of the atheroma and the lipids found in the deposits.

Sites of Atheroma Formation

The localization of the plaques around areas where there are changes in blood flow—e.g. at vessel bifurcations, aortic valve, or where vessels leave the aorta such as at the origin of intercostal, lumbar, renal and mesenteric vessels—suggests that the blood flow is a factor in the origin of the intimal deposits. The occurrence of considerable atherosclerosis in the aortic arch of the control pig with a patent ductus arteriosus emphasizes the importance of changes in blood flow. Some investigators have suggested that the accumulation of minute deposits of platelets[10, 20] and fibrin[21, 22] on the endothelium may be the origin of much of the material found in the atherosclerotic plaque. The blood-flow changes around vessel bifurcations would favour these deposits. Furthermore, it would be reasonable to expect that increased activity of the clotting system would also favour the deposition of platelets and fibrin.

TABLE X.—COAGULATION INDICES FOR THE SWINE IN GROUP A WITH THE MOST AND LEAST ATHEROSCLEROSIS

Material tested in thromboplastin generation test		Activity of serum, $Al(OH)_3$-treated plasma and plasma in the thromboplastin generation test: Incubation time in minutes — 1	2	3	4	5	Russell viper venom time—sec.: Max. ather.	Min. ather.
		Clotting time in seconds						
Serum								
	Mean	13.8	12.1	12.7	15.0	17.4	Mean	
Max. atherosclerosis	S.D. ±	3.8	1.5	2.7	5.3	7.5	16.4	16.6
	S.E.	1.7	0.68	1.23	2.4	3.4	S.D. ±	
							1.4	1.2
	Mean	12.7	16.6	19.1	20.6	24.2	S.E.	
Min. atherosclerosis	S.D. ±	2.5	3.2	6.5	6.3	7.6	0.56	0.48
	S.E.	1.0	1.29	2.60	2.54	3.03		
Plasma								
	Mean	16.0	14.0	14.0	15.5	17.0	Platelet count	
Max. atherosclerosis	S.D. ±	3.2	2.2	3.3	4.1	6.3	No./c.mm. × 1000	
	S.E.	1.46	1.0	1.50	1.86	2.87		
	Mean	25.0	16.2	17.3	21.5	21.1		
Min. atherosclerosis	S.D. ±	18.8	2.8	3.6	5.9	4.9	Max. ather.	Min. ather.
	S.E.	7.5	1.11	1.44	2.36	1.96		
$Al(OH)_3$-treated plasma								
	Mean	14.0	10.8	10.8	11.0	12.0	Mean	
Max. atherosclerosis	S.D. ±	5.2	2.1	2.5	3.7	4.0	336.0	303.0
	S.E.	2.35	0.96	1.13	1.68	1.81	S.D ±	
							64.0	94.0
	Mean	20.0	14.1	12.0	12.0	13.0	S.E.	
Min. atherosclerosis	S.D. ±	19.8	4.9	2.8	1.7	2.2	28.0	38.0
	S.E.		1.96	1.11	0.68	0.89		

Coagulation Indices

In the present study the trends of some of the coagulation indices suggested that the butter-fed group of swine had the more active clotting system. The differences in the clotting mechanism were most marked when the values for the butter-fed animals with the most atherosclerosis were compared with those for the other groups. These butter-fed swine also had a more active clotting system than the butter-fed animals with the least amount of atherosclerosis. This evidence, although limited because of the number of animals used, does suggest that the activity of the clotting mechanism is related to the development of atherosclerosis in swine. Human studies have shown that subjects with atherosclerosis have a more active clotting system than control subjects, and that dietary fat can change the activity of the clotting system.[3, 4, 6, 23] The evidence that the swine with the most atherosclerosis also had the most active clotting system is in keeping with the observations from human studies. Since it has been observed that the phospholipid content of dietary fat is a factor in determining the effect of fat on coagulation,[6] it may have been the phospholipid content of the butter which produced the coagulation changes found in the susceptible swine. Most of the phospholipids are removed from margarine

TABLE XI.—PROBABILITY OF THE DIFFERENCE BETWEEN THE MEAN VALUES OF THE COAGULATION TESTS FOR THE BUTTER-FED SWINE WITH THE MOST ATHEROSCLEROSIS AND THE OTHER GROUPS

	Plasma activity: Incubation time—minutes 1	2	3	4	5	Serum activity: Incubation time—minutes 1	2	3	4	5
AM and B	> .05	.05	.05	.05	> .05	> .05	.01	> .05	> .05	> .05
AM and C	> .05	.05	> .05	> .05	> .05	> .05	.01	> .05	> .05	> .05
AM and AL	> .05	> .05	> .05	> .05	> .05	> .05	.01	> .05	> .05	> .05

	$Al(OH)_3$-treated plasma: Incubation time—minutes 1	2	3	4	5	Platelet count	R.V.V.T.
AM and B	> .05	> .05	> .05	> .05	> .05	> .05	> .05
AM and C	> .05	> .05	> .05	> .05	> .05	.01	> .05
AM and AL	> .05	.05	> .05	> .05	> .05	> .05	> .05

AM = Swine in group A with maximum atherosclerosis.
AL = Swine in group A with least atherosclerosis.
B = Group B (margarine).
C = Group C (no fat).

during manufacture.[24] This may be the reason why the margarine-fed animals showed less atherosclerosis and change in their coagulation mechanism than the butter-fed swine. It does not seem unreasonable to speculate that the increased incidence of atherosclerosis in the butter-fed animals was related to the effect on the coagulation mechanism of the phospholipids in dairy fat which accelerate clotting.

SUMMARY

The changes in blood lipids and blood coagulation and the development of atherosclerosis were studied in 33 swine, divided into three groups, fed either a low fat diet or isocaloric diets rich in butter or margarine. Some atherosclerosis was found in swine on a low fat diet. The high fat diet using margarine as the fat source caused little increase in the amount of atherosclerosis, while a high fat diet containing butter produced a considerable increase in the amount of atherosclerosis. There was no increase in blood cholesterol and phospholipid levels in the swine on the butter or margarine diets. The coagulation indices studied at the completion of the experiment were most active in the butter-fed swine with the most atherosclerosis.

The evolution of the disease and the gross and microscopic findings of the atheroma in swine resembled that found in humans. The evidence from this study suggests that the activity of the clotting system is related to the development of atherosclerosis in swine, and the type of fat fed is an important factor in determining these changes.

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RÉSUMÉ

Les variations de la lipémie et de la coagulation ainsi que le développement de l'artériosclérose furent étudiés chez 33 pourceaux répartis en trois groupes dont le premier reçut la pâtée usuelle, pauvre en graisse et les deux autres une diète isocalorique à base de beurre pour le second et de margarine pour le troisième. On observa de l'athérome même chez les sujets à régime alimentaire à basse teneur graisseuse. Les animaux recevant de la margarine montrèrent des lésions légèrement plus marquées. Par contre, les animaux dont la diète comportait du beurre montrèrent un degré d'artériosclérose beaucoup plus prononcé. Le taux du cholestérol et des phospholipides sanguins demeura sensiblement le même dans les trois groups. A la fin de l'expérience, les facteurs de coagulation les plus actifs furent trouvés chez les animaux nourris au beurre et porteurs des lésions athéromateuses les plus avancées.

L'évolution de l'athérome ainsi que l'apparence macroscopique et microscopique des lésions chez les suidés ressemblent à celles que l'on trouve chez l'humain. Il découle de ces observations que l'activité du système de coagulation semble en rapport avec le développement de l'artériosclérose chez le porc. Le genre de graisse que comporte la diète serait un facteur important dans la détermination de ces changements.

Case Reports

MULTIPLE MYELOMA (LARGE CELL TYPE) IN A 24-YEAR-OLD WOMAN WITH NORMAL TOTAL PROTEIN AND LATENT ELECTROPHORETIC CHANGES

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MULTIPLE MYELOMA is no longer a disease that is diagnosed after all the classical symptoms have developed. The more common usage of bone marrow studies and serum electrophoresis in cases that present minimal radiological changes suggestive but not diagnostic of multiple myeloma, has contributed greatly in this respect.

The reasons for reporting this case are twofold: (1) The young age of the patient. According to a review of cases of multiple myeloma by Lichtenstein and Jaffe, three-quarters of their cases ranged in age from 40-60 years. The disease is not rare in the fourth decade, but few cases have ever been reported in patients under 30. (2) The electrophoretic pattern in which the characteristic changes only appeared two months after the diagnosis was established.

M.E., a 24-year-old coloured woman, was admitted to New York City Hospital complaining of pain in the right flank, spreading to her vertebral column and down the left leg. The pain was intense during move-

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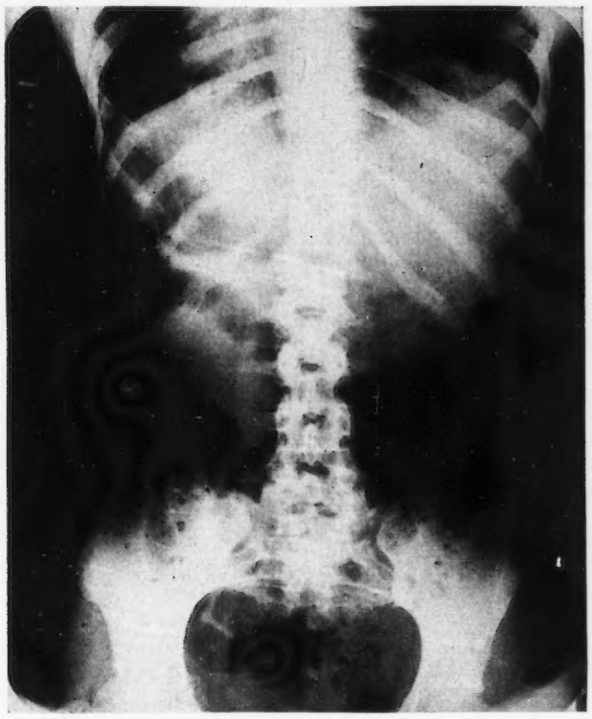

Fig. 1.—Punched-out lesions in the pelvic bones and ribs.

ment or coughing. The only comfortable bed position was flat on her abdomen. The duration of symptoms before hospital admission was one month.

Past record revealed a history of bronchial asthma of ten years' duration and an allergy to sea food. The only operation ever performed was a tonsillectomy in 1945. The family history was vague and non-contributory. Physical examination was normal in most respects. Pulse was 70, blood pressure 130/70 mm. Hg. Pain could not be elicited on percussion or palpation except over the right flank and lumbar region. There was no lymphadenopathy or splenomegaly. The liver was just palpable. Pelvic and neurological examinations were negative.

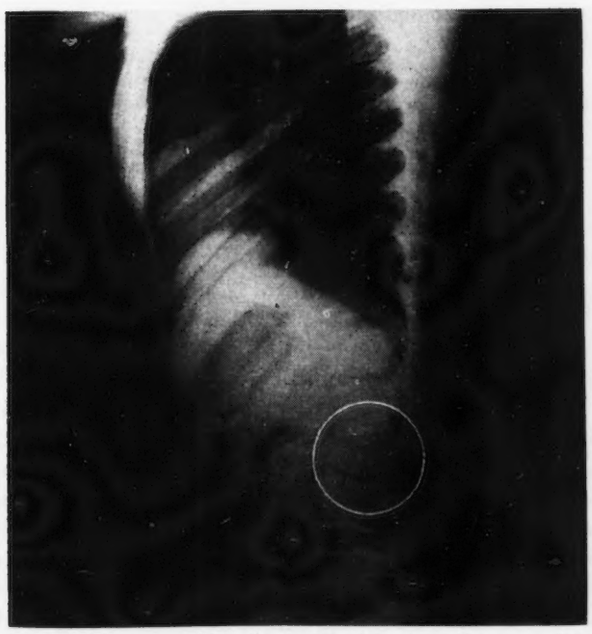

Fig. 2.—Compression and destruction of L4. Note punched-out lesions in the ribs.

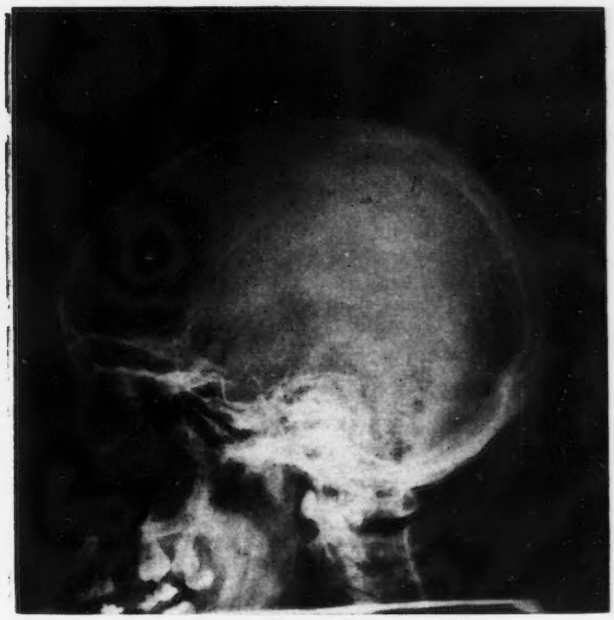

Fig. 3.—Punched-out lesions of the skull.

Radiographs on admission revealed numerous small areas of rarefaction in the bones of the pelvis and upper femora. These were suggestive of an osteolytic process such as multiple myeloma. Several areas of rarefaction were noted in the skull. Ribs showed punched-out, circumscribed areas of rarefaction. The body of the second lumbar spine showed a compression fracture. Intravenous and retrograde pyelography was negative and so were a gastro-intestinal series and a barium enema.

Laboratory Studies

On admission, blood examination revealed a red blood cell count of 3,800,000 per c.mm. No rouleaux formation was noticed. Hæmoglobin 11.0 g. %; hæmatocrit 33%. White blood cells numbered 6000 per c.mm. Segmented leukocytes 64%, juveniles 4%, lymphocytes 32%. Erythrocyte sedimentation rate 42 mm./hr. (Westergren method); bleeding, coagulation and clot retraction times were within normal limits. Urinalysis showed a trace of albumin; Bence-Jones protein could not be demonstrated.

Blood chemistry: B.U.N. 13.4 mg. %; Mazzini test for serology was negative; total serum-protein 7.8 g. % (albumin 4.5 g., globulin 3.3 g.) gamma globulin 11 Kunkel units; serum calcium 10.8 mg. %; serum alkaline phosphatase 3.1 Bodansky units; serum phosphorus 4.8 mg. per 100 ml. Blood sugar and liver function tests were normal. Stool examination for occult blood was negative.

Bone marrow examination revealed moderate cellularity with a relative erythroid hyperplasia. There was a marked increase of plasma cells (20%). Many were large, atypical, with abundant blue cytoplasm and vesiculated nuclei containing nucleoli.

Electrophoretic study of the serum showed no abnormalities in any of the globulin fractions.

Course: The diagnosis of multiple myeloma was entertained, based upon the roentgenologic and bone marrow studies. A second bone marrow examination, performed one month later, showed large clusters of myeloma cells. This finding was considered confirmatory of multiple myeloma. Urethane as well as small doses of

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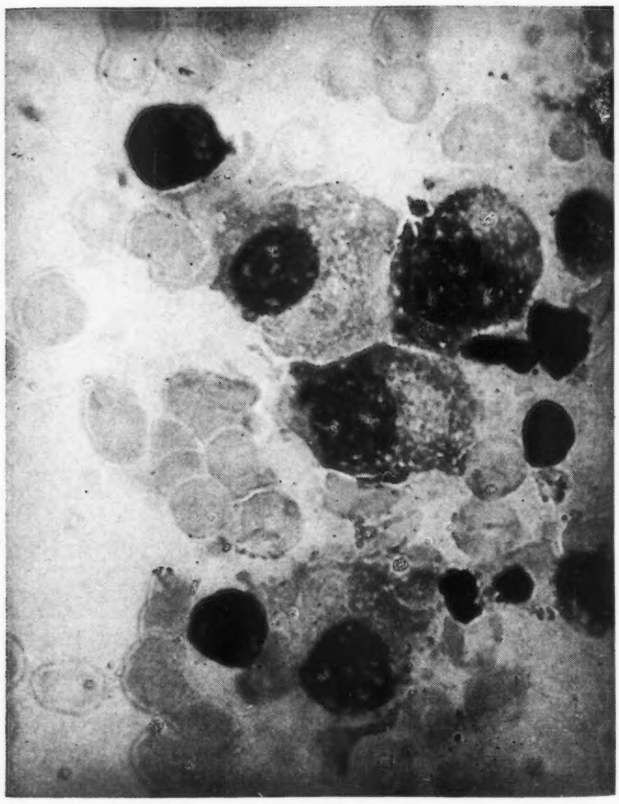

Fig. 4.—Bone marrow aspirate showing cluster of large myeloma cells with eccentric vesicular nuclei.

testosterone was given to the patient. She received whole blood transfusions as supportive therapy. The osteolytic lesions had caused generalized osteoporosis of the lumbar vertebræ, and further lesions in the left humerus and right femur were noted.

Weekly electrophoretic determinations were done. Results remained normal for two months after the initial diagnosis. In the fourth week a homogeneous abnormal globulin corresponding to the mobility of the beta-globulin fraction was noted. Each week the peak of this abnormal globulin increased in height. At the end of two months it appeared as a tall narrow peak with beta-globulin mobility. The total serum protein and total serum globulin never increased. Bence-Jones protein was consistently absent. The patient's condition deteriorated.

DISCUSSION

This case falls into that group of cases of multiple myeloma that do not show hyperproteinæmia. It demonstrated no absolute increase in the total serum globulin or any Bence-Jones protein. Reiner and Stern[2] in studying 91 cases of multiple myeloma demonstrated major anomalies in the electrophoretic pattern in 78% of cases and 22% showed minor anomalies. Adams[3] in his review of 61 cases showed major electrophoretic abnormalities in all but 8 cases, and major and minor abnormalities in 100% of cases. Rice[4] in reviewing 12 cases showed 100% abnormal electrophoretic patterns. Gutman[5] in his review of multiple myeloma developed a scheme of classifying the cases and his Group III contains a small group showing no electrophoretic abnormalities in the protein fraction of the serum.

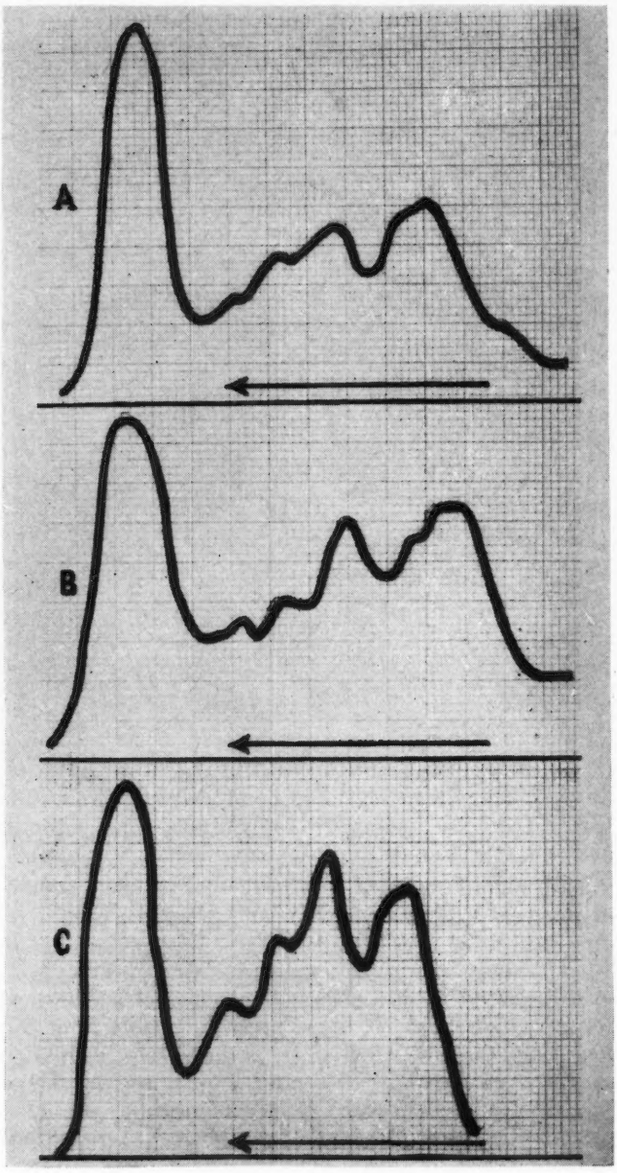

Fig. 5.—Electrophoretic patterns showing the gradual increase of the abnormal myeloma globulin.
A. Shows a normal alpha$_1$, alpha$_2$, beta and gamma globulin.
B. Four weeks later, the myeloma globulin appears in the beta position.
C. Note the marked abnormal peak in the beta position.*
*The pattern below corresponds to this curve. This latter pattern was made two months after the original diagnosis was made.

Knut Aas[6] reported a case similar to ours. Characteristic large myeloma cells were seen. There was no hyperglobulinæmia and no Bence-Jones proteinuria. He, unfortunately, did not have access to electrophoretic studies. Harley[7] reported two cases of multiple myeloma with large myeloma cells without hyperglobulinæmia or any abnormality in the electrophoretic component of the serum. *Bence-Jones protein was present in one case.* Lichtenstein and Jaffe divide myeloma cells into two groups: one with small cells resembling plasma cells, and the second with larger and more varied cell types. In the first group, they state, the serum proteins are normal. In the second, there is hyperglobulinæmia. Our case and the cases of Aas and Harley appear to contradict this hypothesis.

Rundles and associates[8a, 8b] noticed in their study of multiple myeloma that the greater the cellular proliferative activity as judged by the progression of the disease, the greater is the amount of abnormal protein present in the serum or urine. Our case, despite the progressively extensive bone involvement and the large numbers of myeloma cells in the bone marrow, showed no hyperglobulinæmia or Bence-Jones proteinuria.

SUMMARY

A case of multiple myeloma (large cell type) in a 24-year-old woman without hyperglobulinæmia or Bence-Jones proteinuria and with latent electrophoretic changes is presented.

This case points up a fact that is commonly forgotten, namely, that hyperglobulinæmia is not always found in multiple myeloma. A single electrophoretic study may be normal and divert attention from the diagnosis of myeloma.

Electrophoretic patterns should be studied serially if the diagnosis of multiple myeloma is suspected. It may well be that the percentage of cases previously reported to have negative electrophoretic findings would be diminished if serial studies were made. Multiple myeloma can occur in the very young.

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MYCOTIC ABSCESS OF THE BRAIN PROBABLY DUE TO CLADOSPORIUM TRICHOIDES: REPORT OF THE FIFTH CASE*

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IN 1952 BINFORD and associates[1] isolated from a brain abscess a pigmented septate and filamentous fungus which had not been reported before as a cause of disease in man or animals. Emmons,[1] one of Binford's associates, identified this fungus as a new species belonging to the genus of Hormodendrum and gave it the name *Cladosporium trichoides*. Shortly afterwards in the same year, another case of brain abscess due to this organism was reported by King and Collette.[2] The third case was reported two years later from the Belgian Congo by Lucasse,[3] in the brain of a 10-year-old boy. The fourth case of cerebral abscess probably due to *Cladosporium trichoides* was described in 1956 by McGill and Brueck.[4] It should be mentioned that three of the cases occurred in the U.S. and one in the Belgian Congo. Three of them developed in coloured people and one in a white labourer in a rural country. Death resulted in three cases. One case, the first in this series, survived after operation with a good result reported two years later.

Table I summarizes the data in the above-mentioned cases.

The following case is reported because of the similarity of symptoms and signs to those described in the four cases listed in Table I and because of the finding of pigmented segmented branching hyphæ and of pigmented round bodies in a brain abscess.

A 57-year-old Negro was admitted to Westminster Hospital on June 5, 1953, with the clinical picture of malignant hypertension, right hemiplegia and blindness. On admission he was confused and unable even to give his name; the history was therefore obtained from his wife. Apparently the patient was well until 10 months before death when he showed his first symptoms in the form of mental deterioration. At this time his blood pressure was found to be extremely high. Shortly thereafter he suffered a cerebral vascular accident with right hemiplegia. He recovered somewhat but his memory became very poor and he dragged his right foot on walking. Approximately one month later he suffered a second cerebral vascular accident which again affected the right arm and leg, but this time he became incontinent of urine and fæces. The hemiplegia, however, did not involve his face. Soon after he became blind. Six months after the second accident he developed another seizure, with twitching from the neck down and difficulty in swallowing.

On admission he presented a clinical picture of malignant hypertension with a history of three previous cerebral vascular accidents resulting in right hemiplegia. His blood pressure was 230/150 mm. Hg and it was quite labile. Fundoscopic examination revealed marked papillœdema, hæmorrhages and exudate. The lung fields were clear clinically and radiologically. The heart sounds were normal. The temperature was normal. There was no leukocytosis. Blood urea 18 mg. %. C.S.F. and Kolmer-Wassermann negative. Neurological examination revealed ptosis of the right eye with right-sided facial paralysis. The tongue deviated slightly to the right. There was weakness of the right arm and leg. The reflexes were diminished. There was no Babinski or Hoffman response.

He was given Veriloid therapy in the course of which he died suddenly, six weeks after admission.

Post-Mortem Examination

Autopsy was performed 11 hours after death. The body weighed 119 lb. (54 kg.) and measured 68.5 in. (174 cm.) in length. The principal gross findings were confined to the brain. The left cerebral hemisphere was larger than the right, and a definite fullness was palpated in its posterior portion. On incision of this

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TABLE I.

Case No.	*Described by*	*Age, sex, race*	*Symptoms and signs*	*Operation*	*Autopsy findings*
1	Chapman	22, coloured man	Frontal headache, drowsiness, convulsions	Abscess of the left frontal lobe	*
2	King and Collette	47, white man	Right hemiplegia, hypertension	Abscess of the left frontal lobe	Recurrence of fungus infection
3	Lucasse	10, coloured boy	Blindness, epileptic fits	—	Small abscess of the brain with invasion of ventricles by fungus; hydrocephalus
4	McGill and Brueck	37, coloured woman	Right hemiplegia	Abscess of the left parietal lobe	Mycotic abscess of brain

*Survived.

area a rounded abscess cavity, the size of a golf ball, was found at the junction of the left parietal and occipital lobes (Fig. 1). Just in front of this abscess there was a large area of softening involving the internal capsule, and slightly lateral to it there was a peculiar rounded structure with a central lumen which resembled a sinus tract. This structure was about the size of a lead pencil. The abscess contained thick yellowish-green purulent material. The cerebral convolutions were flattened, indicating the presence of elevated intracerebral pressure. The arteries at the base of the brain presented a severe degree of atherosclerosis, particularly prominent in the middle cerebral arteries. The right middle cerebral artery showed a lumen reduced to pin-point size, while the left middle cerebral artery showed stenosis to a slightly less marked degree. There was no evidence of occlusion of the cerebral arteries by either thrombus or embolus. The other autopsy findings were moderate cardiac hypertrophy (430 g.), and a moderate grade of atherosclerosis of the coronary arteries. An intimal hæmorrhage was found in the right coronary artery. Acute ulcers of the gastric mucosa were also seen; they were considered to be neurogenic in origin.

Microscopic Examination

Microscopic examination of the cerebral abscess showed it to be lined by proliferating spindle shaped cells having a superficial resemblance to epithelioid cells (Fig. 2). Numerous giant cells were present in this lining membrane, and in these definite branching segmented brown hyphal segments and brown round septate bodies were found (Fig. 3). There were numerous pigmented fungi in the purulent material as

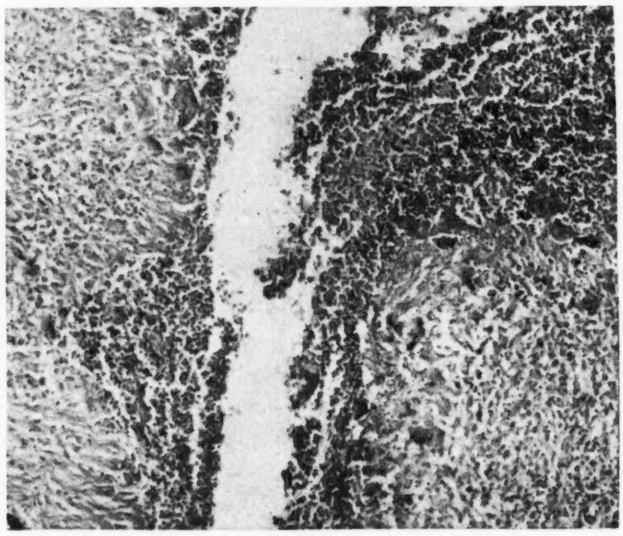

Fig. 2.—Low-power photomicrograph of the abscess and sinus tract in the left parieto-occipital lobe. The epithelioid cell lining with foreign body giant cells is shown. H. & E. × 70.

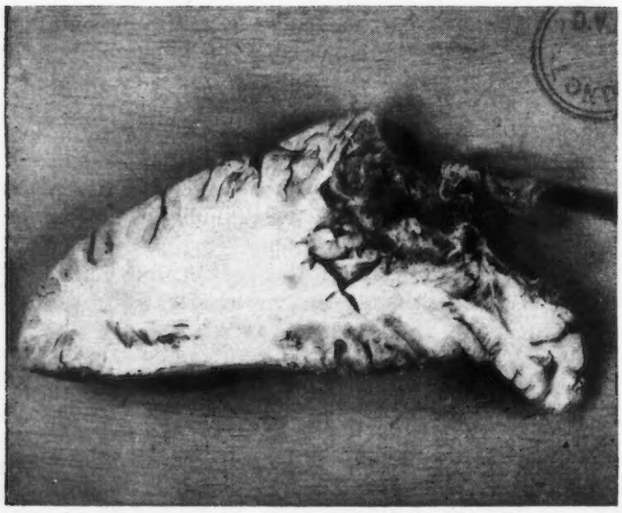

Fig. 1.—Photograph of gross vertical section of the abscess in the left parieto-occipital region.

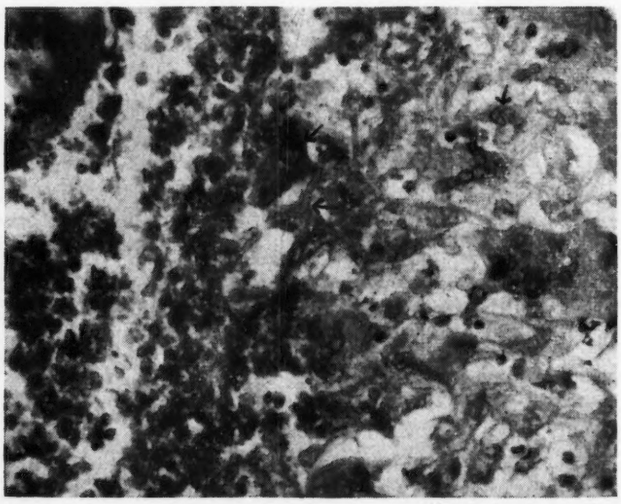

Fig. 3.—High-power photomicrograph of the giant cells and epithelioid cells lining the abscess. The arrows point to the branching hyphæ and to the rounded septate bodies. H. & E. × 400.

well as in the necrotic tissue in the area of softening. The inflammatory cells consisted mostly of plasma cells, lymphocytes and polymorphonuclear leukocytes. Sections taken through the optic chiasma revealed the presence of similar fungi, but none was found in the lungs or other organs. It is to be particularly stressed, however, that no mycological cultural studies were done; after routine culture media inoculated with pus from the cerebral abscess had revealed a light growth of *Staphylococcus aureus*, all of the material was discarded. Microscopic examination of the kidneys revealed lesions of benign nephrosclerosis.

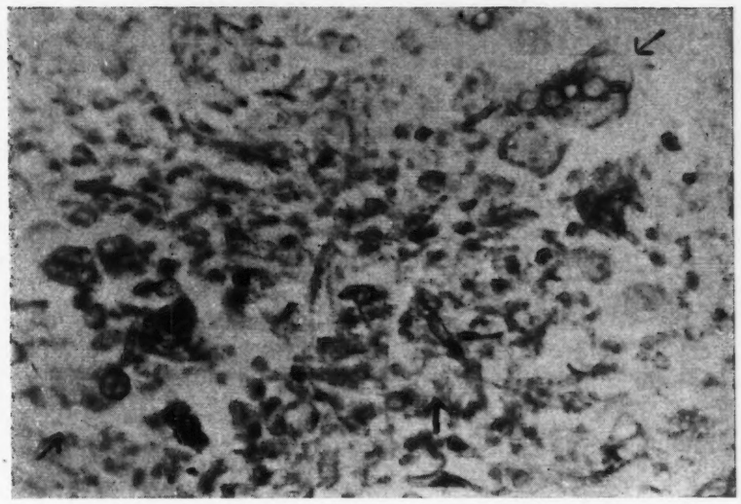

Fig. 4.—Microscopic picture is identical with that in the proven case of *Cladosporium trichoides* infection described by Lucasse and associates.

DISCUSSION

This mycotic abscess of the brain was caused by a fungus which morphologically appeared in the tissue in the form of brown segmented branching filaments, 2-3 μ. in diameter, and of round brown septate bodies. The diameter of the round bodies, which might have represented so-called chlamydospores, was 9 μ. These round bodies were found in the hyphæ and their position was therefore intercalary. The fungus was found in giant cells as well as mixed with tissue debris. It is to be noted that pigmented septate round bodies of approximately the same size, but not in association with pigmented segmented hyphæ, have been seen in skin lesions of chromoblastomycosis.[5(a)] In the differential diagnosis of those cerebral mycoses which may show round bodies and branching segmented mycelia, *Candida albicans*[5(b)] and *Geotrichum candidum*[5(c)] should be considered. However, these organisms are not pigmented and their round bodies whenever formed are not septate. No fungus other than *Cladosporium trichoides* has been described which produces pigmented septate round bodies and pigmented branching hyphæ in tissues. The fungus shown in Fig. 3 closely resembled morphologically that obtained from the brain of a 10-year-old boy from the Belgian Congo and illustrated in Fig. 4 (reproduced by courtesy of Lucasse, Chardome, Magis and Vanbreuseghem). A definite diagnosis in the present case rests, of course, on the isolation of the organism in culture. Unfortunately, no mycological studies were carried out in this case. If they had, the growth of *Cladosporium trichoides* on Sabouraud's media would have appeared at room temperature in approximately six days with the production of dark brown to black felt-like colonies. The fungus is known to grow well at room temperature as well as at 37° C. When preparations from such cultures are examined microscopically, brown hyphæ and conidiophores bearing long sparsely branching chains of conidia should be observed. The conidia should be brown and elliptical, 2 to 2.5 by 4 to 7 μ. in diameter. When inoculated intravenously into mice and rabbits, fatal cerebral lesions should be produced.[1]

Several points of interest arise from the present case:

1. A mycotic abscess of the brain due to a pigmented fungus of the genus Hormodendrum, probably *Cladosporium trichoides*, was found unexpectedly at autopsy in a hypertensive patient.

2. The mycotic brain lesion was probably responsible, in part at least, for right hemiplegia and blindness.

3. No morphological evidence of fungus was found in any other organ; however, cultural techniques were not used. No portal of entry was established in the present case or in the four other cases reported in the literature.

4. This case was observed approximately one year after the first report on this type of infection by Binford.[1]

5. This case illustrates the vital importance of culturing material from brain abscesses for fungi as well as for bacteria.

SUMMARY

A mycotic abscess of the brain probably due to *Cladosporium trichoides* (Emmons, 1952) is described. Hemiplegia and blindness resulted.

I wish to express my thanks to Dr. J. C. Paterson, Chief of Laboratory Services, Westminster Hopital, London, Ontario, for assistance in the preparation of this report; to Mr. D. Pulhem for the illustrations; and to Prof. R. Vanbreuseghem of the Institute of Tropical Medicine, Antwerp, for permission to reproduce the microphotograph of the case from the Belgian Congo.

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GANGRENE AS A COMPLICATION OF MALROTATION WITH VOLVULUS

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THE EMBRYOLOGICAL development of malrotation of the large bowel is well described by Ladd and Gross[1] and also by Aldrich.[2] To summarize these accounts in a few words, it is usually anomalies of the second stage of midgut rotation that give rise to non-rotation and malrotation with their complications of obstruction and/or volvulus.

The following case illustrates malrotation with volvulus of the small bowel and gangrene.

A white male infant, born on December 17, 1956, with the aid of low forceps, cried spontaneously and his colour was good. Birth weight was 7 lb. 2½ oz. External examination was negative and the appearance was that of a healthy baby. He retained his first few feedings, but on the third neonatal day he had green vomitus and mucous stools. The next day regurgitation continued and the stools were bloodstained. Hæmoglobin level fell from 19.6 g. % to 11.1 g. %. The baby continued to vomit and have loose stools containing blood.

On December 21, four ounces of a dilute barium mixture was given and films were made after 25 minutes and reported on as follows: "The œsophagus is dilated with barium; the stomach is large, as is the duodenum. There is an abrupt arrest of the barium, probably in the second part of the duodenum; this ends in a broad base with a tapered point, the appearance being that of stenosis.

"A film made after three hours shows that about 7½ cm. of the duodenum has a lumen of not more than a thread in diameter. Beyond this the barium has filled the bowel for another 10 cm. There is very little gas in the remainder of the bowel."

Following the x-ray examination the stomach was emptied by suction. Glucose in water was given interstitially, also penicillin intramuscularly in preparation for operation. Laparotomy was performed through a four-inch right paramedian muscle splitting incision. On opening the peritoneum, the cæcum and appendix presented. The small bowel was bluish, turgid and rotated on a short mesentery. On delivering the small bowel into the wound, the upper four inches (10 cm.) of the jejunal wall was necrotic in patches of various sizes, not larger than 1 x ½ inch. The rotated bowel was reduced in a counterclockwise direction, and a Ladd's procedure released the obstructing band from the cæcum to the lateral peritoneal wall. Gas and fluid then flowed freely into the jejunum.

The necrotic portion of the jejunum was extensive enough to require resection. The cut ends of the bowel were inverted by purse string and oversewn. A side-to-side two-layer anastomosis was done and the mesenteric defect was closed. After the patency of the anastomosis had been checked, the abdominal wound was closed in layers.

After operation the baby was placed in an isolette. Oxygen was administered periodically for moderate cyanosis. Thirty c.c. of blood and 70 c.c. of glucose and saline were given intravenously in the subsequent 24 hours. Two ounces of normal saline were instilled rectally twice daily. On the second postoperative day, gastric drainage was discontinued and glucose feedings were started. Formula was given on the third day and retained. The rectal temperature ranged between 101 and 102° F.

On December 26, the weight was 6 lb. 10 oz. X-ray examination on January 9, 1957, with barium meal showed the anastomosis to be functioning well. The infant was discharged on January 15, 1957, 29 days after birth and 23 days postoperatively. The discharge weight was 7 lb. 4 oz.

Investigation of the literature revealed only two cases of resection of gangrenous small bowel in the newborn with survival. Moretz and Morton[3] reported a male born by hysterotomy who showed signs of intestinal obstruction on the second neonatal day. Operation revealed a volvulus of 15 cm. of ileum 12 cm. from the ileo-cæcal valve around a congenital band from the liver to the right lower quadrant. The involved ileum was gangrenous, and resection was done with end-to-end anastomosis. After a critical period he was discharged four weeks after operation.

David Charles[4] reported the case of an infant born by hysterotomy who developed intestinal obstruction on the third neonatal day. Obstruction was due to malrotation and volvulus of the terminal ileum in the region of the ileo-cæcal valve. The ileum was gangrenous and was resected. The child died on the 14th day from massive intestinal hæmorrhage.

Since the time of this survey, a further reference has been obtained by personal communication. Beattie[5] is reporting, in a paper not yet published, two cases of small bowel gangrene occurring as a result of midgut volvulus. The first was in a four-week-old white male with 50 cm. of necrotic jejunum, which was resected, with survival. The second was in a six-week-old coloured male with gangrenous small bowel which was resected, after which he developed pancreatitis and further extension of gangrene to involve most of the small bowel. Death occurred on the 20th postoperative day.

The mortality in cases of malrotation is increased when volvulus is also present. Other associated complications raise the mortality to nearly 100%. Aldrich[2] collected 14 cases, six in males and eight in females, of malrotation or non-rotation, seven associated with volvulus of the small bowel. Thirteen of these cases were operated upon, at ages ranging from one week to twelve years. There was arrest of normal rotation in eleven, lack of rotation in two, and reverse rotation in one. Of the 13 who were operated upon seven survived. Four of the fatalities were associated with volvulus. Ladd and Gross[1] reported on 156 cases of malrotation. With

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malrotation alone 85% survived but when malrotation was complicated by other abnormalities the survival rate fell to 43%; none of these complications involved gangrene with resection.

The signs of midgut volvulus are:

1. Vomiting of bile.
2. Bloody discharge from the rectum.
3. A silent abdomen.
4. Abdominal distension.

X-ray findings:

1. Flat and upright films show multiple dilated gas filled loops.
2. Barium enema shows arrest at the mid transverse colon.
3. If dilute barium mixture is given by stomach tube, the stomach and first and second portions of the duodenum fill and are distended.

There is seldom any contraindication to giving well-diluted barium by the above method if two precautions are taken: firstly, empty the stomach by lavage before administration of the meal; secondly, after all necessary radiographs have been taken, aspirate the stomach and duodenum repeatedly.

All the signs and x-ray findings may not be present. If the obstruction is high and it is early in the neonatal period, there may be minimal gas in the ileum and large bowel. In our case there was very little distension and the films of the abdomen did not show large gas-filled loops of bowel (I believe, for the above-mentioned reasons).

SUMMARY AND CONCLUSIONS

Malrotation results from a failure of proper embryological development. Excellent accounts of these failures have been given by various authors. Malrotation of the midgut is not too common, but when it does occur it often gives rise to volvulus and obstruction.

Gangrene is due to obstruction of a collateral of the superior mesenteric artery and may involve all of this arterial supply.

Vomiting of bile and the appearance of blood in the stool are indicative of obstruction and demand x-ray investigation.

Treatment is operative, with release of the band which stretches from the cæcum across the duodenum to the lateral peritoneal wall. Further procedures are dictated by any complications found at the time.

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Special Article

THE CANADIAN ASSOCIATION FOR RETARDED CHILDREN

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It is unlikely that . . . . there is any other form of disability which equals impairment of mental ability in respect to its toll of economic uselessness and human misery. If one uses as the criterion of disability the inability to obtain gainful employment, one can say that, with the possible exception of mental illness, mental retardation is the most significant handicap of our present society.
—RICHARD L. MASLAND[1]

ON JANUARY 31, 1958, the Canadian Association for Retarded Children received its Letters Patent from the Secretary of State. This represents a milestone in the development of the national organization which the parents and friends of retarded children have endeavoured to establish. It also prompts some reflections on community programs for the mentally retarded in this country.

There will be general agreement that mental retardation is one of the foremost challenges to the medical profession in our time. In regard to the number of patients involved, it ranks first among the chronic disabilities of childhood. Estimates of its precise incidence in different countries vary widely according to the criteria employed. However, they all demonstrate the recognized peak incidence at 5 to 14 years of age, and it can be safely stated that *at least* 1% of all children under 18 years of age have an intelligence quotient of less than 75.[2] The English educational system aims to make provision for 1% of school children in special schools, while a further 8 or 9% are considered to require special educational provision within the ordinary school system.[3] Both in Britain and in the United States conservative estimates indicate that about 1% of the total population and 2 to 2½% of school-age children are mentally retarded.[4-6] On the basis of the 1956 Dominion Bureau of Statistics Census, these figures, applied to Canada, would suggest that: (a) there are over 150,000 retarded persons in this country; (b) at least 50,000 of these are children aged 5 to 14 years; (c) with the increase in population and longer life span of these children the total number of retarded in this age group will probably rise by at least 1000 annually.

It seems fair to say that, in the past, communities everywhere have been somewhat slow to face this problem and to accept responsibility for it. The chief measures taken were the establishment of residential institutions for the retarded. In Canada, the care and training of mentally defective persons is primarily a provincial responsibility, and therefore the provincial governments have established and maintained these institutions (though there are none as yet in New Brunswick, Newfoundland and Prince Edward Island).

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Since the Second World War there has been a tremendous upswing of interest in retarded children almost simultaneously all over the world.[7, 8] It should be frankly admitted that this appears to be due primarily to the increased activity of the parents rather than that of the medical or teaching professions. The movement started as groups of parents banded together, and usually their first project was to establish a special school for "trainable" children. The mildly retarded are now generally taught in the public school system where the number of special classes is gradually increasing; the severely retarded are mostly in institutions. The moderately retarded, with an approximate intelligence quotient of 20 to 50, form the intermediate group, and their instruction represents a community problem as they can usually be kept at home in their early years but have not been considered "educable" within the public school system. It is for these children that the parent groups first established special schools, often in church halls or other inexpensively rented premises.

One of the first special schools in Canada was the one at Kirkland Lake, Ontario, which was opened in 1947. Gradually others followed. As the parent groups increased in number they joined together in provincial organizations and began to press for financial assistance to their schools from school boards and provincial departments of education. The claim for such assistance can hardly be denied; the World Health Organization[3] has stated quite clearly that: "The education of all children, both normal and subnormal, should be the responsibility of the educational authorities, and no artificial barriers should be erected between normal children and those for whom special provision has to be made. . . ." In many provinces the associations for retarded children were, in fact, greatly assisted by their government departments of education and also the departments of health and welfare, and the mental health services. Ontario first passed special legislation in 1954 to assist the cost of education of retarded children, and other provinces followed. This financial aid gave a great impetus to the development of special schools, and further assistance came from service organizations and other voluntary agencies. By now there are over 100 special schools in Canada—46 in Ontario alone and 31 in British Columbia.

The parent groups have gradually developed a variety of other functions apart from the establishment and maintenance of these special schools and the raising of funds for them. The groups have regular meetings at which the members share their experiences, attend lectures, view films, and discuss the problems of their organization. They have educational, recreational and publicity programs. They are usually concerned with the transport arrangements for the children attending their schools. Many chapters have libraries. Some have attempted to organize kindergartens for the younger children and simple sheltered workshops for the adolescents. Most chapters have medical and educational advisers.

Some groups have been able to embark on more ambitious projects. Thus, several have acquired their own school buildings, and completely new schools have been built, for instance by the South Waterloo Association at Galt, Ontario, and the Upper Fraser Valley Society for Handicapped Children at Chilliwack, British Columbia. In Ontario and Alberta capital grants for such school buildings have been obtained from government or municipal sources. Other parent groups are beginning to concern themselves with the creation of private residential facilities, sometimes for children attending day schools whose homes are too distant for daily travel, or as short-stay hostels in times of family crises.

By now these chapters are linked together in a provincial organization in each of Canada's ten provinces. The provincial bodies have somewhat different functions from the individual parent groups. They are not concerned with the maintenance of schools and have to do little direct fundraising. They act rather as a co-ordinating council for all their local groups and encourage the formation of new ones. They also have more widespread educational and publicity programs, and they endeavour to influence provincial legislation in favour of retarded children. Usually they interest themselves in the training and qualifications of teachers for the retarded, and several provincial organizations have organized summer courses for these teachers in conjunction with their provincial departments of education and sometimes with the local universities. They may also establish an auxiliary for their provincial residential school in co-operation with the local chapter concerned. In Ontario, the provincial association organizes a summer camp for retarded children and has made an enlightening film of it. The larger provincial bodies have also begun to interest themselves in research; thus the Ontario Association has financed a project under Dr. Norma Ford Walker. Usually these associations have an advisory board of medical, educational, legal, financial and other experts. Perhaps the arrangement in British Columbia is most suitable where the medical advisory committee has separate meetings and has a representative on the executive committee of the provincial association, for medical advisers representing several specialties are usually involved and can discuss their advice most freely among themselves.

In July 1956, the first out-patient clinic for retarded children in Canada was established at the Montreal Children's Hospital, with financial assistance from Federal Health Grants and also from the Association for the Help of Retarded Children (Quebec) Inc.[9] Similar clinics have been established in several cities in the United States and in Europe.[10-12] They are of great value to retarded children and their parents, and their location in hospitals with first-class diagnostic facilities also promotes research and professional interest in mental retardation. Ultimately each province should perhaps have at least one such clinic, and in addition, a travelling clinic should be available.

As the provincial societies developed, the need for an overall Canadian organization became apparent. In May 1955, representatives of several provincial associations met in Toronto to discuss ways of joining together. This was followed by a more formal meeting in Winnipeg in January 1956 when a constitution for the Canadian Association

for Retarded Children (C.A.R.C.) was worked out in detail and the first officers were elected provisionally. In September 1956 this Association held its first annual meeting in Toronto. A further general meeting took place in Calgary on September 17 to 19, 1958, together with a conference on mental retardation.

The Canadian Association is essentially a federation of provincial associations; the members of each provincial association constitute the individual membership of the C.A.R.C. and vote through their delegates. There are now over 12,000 such individual active members in over 100 chapters in the ten provinces. The functions of the national body are somewhat similar to those of provincial organizations, but on a federal level. Thus the Canadian Association is to co-ordinate the efforts and activities of parents' groups and provincial bodies, and is to assist in their establishment. It has only a limited direct fund-raising program and is largely dependent on subscriptions from the provinces; however, it plans to organize nation-wide publicity and fund-raising campaigns in conjunction with the provincial organizations and their chapters. It hopes to serve as a clearing-house for information to the general public and to co-operate with other national organizations for the handicapped. It will endeavour to influence federal legislation on behalf of retarded children and will interest itself also in the training and education of suitable personnel for their care. Finally, it particularly wishes to further research into mental retardation on a nation-wide scale. A number of committees and advisory councils are being formed to guide the Association in these various fields, and the particular importance of close contact with the medical profession is fully realized.

The C.A.R.C. is still in its infancy. The potential importance of such a nation-wide organization can best be seen by reference to the National Association for Retarded Children (N.A.R.C.) in the United States. That Association was founded in 1950, and it took time to gather strength, but now it has become an influential organization with over 500 chapters. It publishes a bi-monthly newspaper, "Children Limited", and has had considerable effect on federal legislation. In 1956 the following events occurred:

1. The President of the United States mentioned for the first time the problems of mentally retarded children in his annual State of the Union Message as an unmet need in the area of social welfare.

2. A bill specifically formulated to help in the training of teachers of the mentally retarded was passed by the Senate.

3. Congress appropriated $3,500,000 specifically for the retarded. This included $2,000,000 to the Children's Bureau for diagnostic and treatment clinics throughout the country; $675,000 to the Office of Education for research on a co-operative basis with universities and State departments of education; and $750,000 to the National Institutes of Health for assistance to medical and other research.

4. The Ford Foundation awarded $450,000 to Dr. Linus Pauling for a research project at the California Institute of Technology, concerning the biochemical aspects of mental retardation. The Rockefeller Foundation also gave substantial sums for research in this field.

5. The Association itself set aside over $73,000 for research, nearly one-third of its budget for 1956-57. Over $51,000 of this sum was for medical research and was made available to the Advisory Board.

Meanwhile the N.A.R.C. had appointed Dr. Richard L. Masland, Professor of Neurology, Bowman Gray School of Medicine, Winston-Salem, N.C., as its research director. Dr. Masland embarked on an extensive survey of the research which is being carried out in the field of mental retardation at medical centres in Europe and America. His valuable report has just been published.[1] The N.A.R.C. also supported relevant research in psychology and anthropology by Drs. Seymour Sarason and Thomas Gladwin.[13]

In view of the greater population and wealth of the United States, it must not be expected that the C.A.R.C. can achieve as much as the N.A.R.C., but there are good prospects of increased private and government interest in the retarded in this country, too.

Finally, a few comments may be made concerning research in Canada as the C.A.R.C. is eager to promote this. The investigation of the causes and treatment of mental retardation is, of course, not purely a medical matter. It involves work by physicians, geneticists, psychologists, social workers, biochemists and a variety of other scientists, often in teams. In addition, there is a field of research in regard to perceptual, intellectual and behavioural characteristics and growth patterns, learning ability, and optimal educational methods in various types of retarded children; this involves chiefly psychologists and educators. The complexity of the various approaches to the subject can be seen from a list of American research projects now in progress.[14] At present the difficulty is not so much to find funds for research as trained personnel. In November 1957 the C.A.R.C. invited Dr. Masland to speak in Toronto and Montreal concerning the results of his survey. He stressed two important practical points: first, the need for more research posts in academic centres with long-term economic support for persons willing to devote their lives to such studies, and secondly, the need to have future programs for the retarded planned and located in close association with teaching and research centres. Medical schools should have affiliated diagnostic centres for the mentally retarded, and residential institutions should be so located as to make it possible for consultants and residents from the medical centres to have appointments in the training schools.

These are matters to which much attention will have to be paid in the future if the challenge of mental retardation is to be met.

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SHORT COMMUNICATIONS

A COMPARISON OF INTRAVENOUS CALCIUM DISODIUM VERSENATE AND ORAL PENICILLAMINE IN PROMOTING ELIMINATION OF LEAD*

CECIL E. C. HARRIS, B.Sc., M.D.(Glas.), F.R.C.P.(Edin.), *Montreal*

DIMERCAPROL (British Anti-Lewisite, B.A.L.) has been used in the management of poisoning with some heavy metals, and it appears to exert its effect by virtue of possession of two thiol groups which compete with tissue thiol groups for the metallic element concerned. Walshe in 1953[8] described a compound β,β-dimethylcysteine, known now as penicillamine, which is excreted in the urine of patients to whom penicillin is being given. This substance is in the reduced (-SH) form in which it is stable, highly soluble and of low acute toxicity.

Wilson's disease (hepato-lenticular degeneration) is associated with a positive copper balance and an accumulation of this metal in the tissues of the body. On an analogy with the chemical structure of dimercaprol, Walshe was inspired to try the effect of penicillamine in this disease on the theory that the thiol group might be active in chelating copper and thus in promoting its urinary excretion. Penicillamine being administered orally, it would, if effective, spare the patient the often painful intramuscular injections necessary with dimercaprol therapy. Walshe[9, 10] found his anticipations to be realized and he was able with conspicuous success to undertake long-term treatment of patients with Wilson's disease. Confirmation of his experience was provided by Fister, Boulding and Baker[3] who recorded, for example, the case of a child in whom continuous administration of penicillamine for eight months so depleted the abnormally high copper content of the body that marked clinical improvement was a consequence; these workers suggest that, in the absence of material ill-effects and with certain precautions, such treatment may be maintained for months or even years. One theoretical objection is that prolonged administration might interfere with normal cysteine metabolism and lead to hepatic necrosis; no such complication has as yet occurred in practice.

Dimercaprol is dangerous to use in lead poisoning because the BAL-lead complex formed is itself toxic and may precipitate encephalopathy. Walshe suggested that penicillamine might prove of value in other metallic poisonings, including plumbism. Boulding and Baker[2] reported considerable increase in urinary lead excretion in two cases of lead poisoning when penicillamine was administered, and thought that available evidence indicated this substance to be therapeutically superior to the other chelating agent in use, namely, calcium disodium ethylenediamine tetra-acetate or versene. For convenience in this paper the latter will be referred to as "versenate".

Advantage was taken of a recent minor flurry of cases of plumbism in Montreal to combine active treatment with a comparison of the effectiveness of intravenous versenate and oral DL-penicillamine. Two patients in whom adequate studies were completed will be described. The versenate was given as a 5 ml. dose containing 1 gram of the salt and diluted in at least 250 ml. of glucose-water; administration was twice daily and at least an hour was taken for each infusion. Penicillamine was given orally ½-1 hour before meals in dosage of 0.3 g. in gelatin capsules thrice in the day.

The total urinary output was collected and measured in lead-free containers. After mixing, samples were analyzed for lead content and the total daily excretion could then be calculated. For each patient an initial control period was followed by administration of one of the two agents. An intermediate period without treatment preceded use of the other agent and the trial concluded with a final control period. In one case, versenate was given first and in the other penicillamine was used initially.

CASE 1

G.G., a husky man of 27 years, was admitted on March 20, 1958. He had worked for seven years in a foundry making bronze (an amalgam of copper and lead). He had been transferred four months previously into the furnace room in which molten lead gave off fumes. For two months he had suffered increasing abdominal colicky discomfort with occasional

*From St. Mary's Hospital, Montreal.

vomiting and some diarrhœa; he had also noted cramps in the muscles of his right arm. There were no other relevant facts in his story, and physical examination was negative apart from a "blue line" at parts of his gum margins and some doubtful neurological signs. Various investigations were carried out to exclude, for example, organic gastro-intestinal disease, and no lesion other than plumbism was found. Confirmation of the latter diagnosis was provided by the slight anæmia (hæmoglobin level 13.6 g. %) with 6.4 stippled cells per 1000 red cells, by the high blood lead level (0.114 mg./100 ml.); normally 0.01-0.07 mg.) and by the raised lead content of the urine (0.46 mg./litre; normally 0.02-0.10 mg.). Initially he was given calcium lactate to suppress symptoms and then, from March 27 to 31, he had five days of versenate therapy as previously outlined. He was discharged temporarily on April 1, the hæmoglobin level having fallen to 12.8 g. % and minor symptoms persisting, colic in particular. He was readmitted on May 1 with a hæmoglobin level of 15.2 g. %, his red cells being free from stippling. His urinary lead excretion was 0.364 mg. in a 24-hour test period. The effects of versenate and of penicillamine upon urinary lead excretion are shown in Table I.

TABLE I.—PATIENT G.G.

Day	*Treatment*	*24-hour urinary lead excretion mg.*
1	Nil	364
2	Versenate	2692
3	Versenate	2064
4	Nil	502
5	Penicillamine	1748
6	Penicillamine	1545
7	Nil	457

CASE 2

B.A., a pale 25-year-old man, was admitted on March 26, 1958. He had worked for five years at the same foundry as the previous patient and had been moved into the furnace room one year before admission. For three months he had noted progressive fatigue with muscular weakness at the end of a day's work. No change had occurred in his habitual constipation. There had been no abdominal symptoms. There were no other relevant points in his history. Examination showed a "blue line" along some portions of his gums; there were no other abnormal physical findings. Anæmia was present, the hæmoglobin level being 11.2 g./100 ml., and there were 8.2 stippled cells per 1000 red cells. The blood contained 0.093 mg. lead per 100 ml. and the urine contained 0.248 mg./litre. A high calcium intake for a few days had little effect on his symptoms and he was given a course of versenate from April 2 to 6. He was then temporarily discharged to be followed up as an outpatient. Readmission on May 1 found him with a hæmoglobin level improved to 15.2 g. % and he was free from symptoms. However, a control period showed the urinary lead still to be high, 0.252 mg. being excreted in 24 hours without treatment. The effects of versenate and of penicillamine are portrayed in Table II. During the period of treatment there was a return of minor cramps in limb muscles.

TABLE II.—PATIENT B.A.

Day	*Treatment*	*24-hour urinary lead excretion mg.*
1	Nil	252
2	Penicillamine	1777
3	Penicillamine	2150
4	Nil	1260
5	Versenate	2455
6	Versenate	2575
7	Nil	1440

DISCUSSION

Plumbism is much less common than previously, and Hunter[4] provides for the interested reader a detailed account of the historical background and of the preventive measures responsible for lowering the incidence of this particular industrial hazard. Workers are, however, still at risk, and human nature is such that overt cases of plumbism will continue from time to time to present themselves. This being so, the question of treatment must still be kept alive; a quotation from Hunter's treatise, published in 1955, is pertinent:[5] "The ideal method to increase the excretion of lead from the tissues is still being sought." Potassium iodide, ammonium chloride and sodium citrate are now only of historical interest. Dimercaprol involves the risk of lead encephalopathy; in addition, the intramuscular injections are often painful. The use of versenate intravenously raises obvious practical problems, particularly if long-term therapy is contemplated; furthermore, this treatment is not free from danger.

As elimination of lead with either versenate or penicillamine appears to be of the order of only some 2 mg. a day and as post-mortem studies of lead workers show a total body content of 200-800 mg., prolonged "de-leading", especially of those who show symptoms of poisoning, would seem desirable. It is for this reason that penicillamine, orally effective and seemingly quite harmless, may approach the "ideal method" sought by Hunter. Obviously it would be quite unnecessary completely to remove all the lead from a case of plumbism, but, even so, treatment might be better continued for weeks or months, probably with intervals without medication. The question also arises as to the advisability of giving short courses of "de-leading" periodically to workers exposed to the hazard, to prevent accumulation in the tissues. Economic factors are worthy of note. Penicillamine may be obtained at present for about $3.50 per gram, sufficient for one day of treatment; should demand increase and "mass production" prove possible, the price may well fall in the future. Versenate also costs about $3.50 for a day's supply of two ampoules each of 5 ml., but the provision of facilities for intravenous therapy must be added to the expense.

It is proposed to seize the next opportunity of comparing in a similar fashion penicillamine with versenate given orally. It is known that this latter

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approach is being employed, but published work is meagre. Bidstrup[1] mentions that versenate is poorly absorbed from the gut, but Pagnotto, Elkins and Bayka,[7] while admitting that only some 3% of orally administered versenate can subsequently be recovered from the urine, point out that this is sufficient in theory to combine with about 7 mg. of lead. The latter authors feel that versenate should be as effective by mouth as it is by the intravenous route.

Leckie and Tompsett[6] provide an exhaustive review of the mechanisms involved with chelating agents. They emphasize that, in doubtful cases of heavy metal poisoning where excretion is at borderline levels or even lower, greatly increased excretion following the use of one of these agents may give invaluable confirmatory evidence.

CONCLUSIONS

Intravenous versenate and oral penicillamine both produce an increase in lead excretion in cases of plumbism. Elimination in the patients studied was slightly greater with versenate than with penicillamine, but it is felt that the ease of administration of penicillamine and its lowered toxicity combine to outweigh the trifling superiority of versenate in this regard.

Comparison of oral versenate with penicillamine is a desirable future study.

Dr. Mary Morrow introduced me to Dr. J. E. Boulding who made several helpful suggestions. Dr. R. Moralejo kindly referred the patients to my care. Dr. G. E. Joron supplied constructive criticisms of initial drafts of the paper. I am indebted to Dr. F. J. Tourangeau and to Mr. J. P. Paré, M.Sc., of the Division of Industrial Hygiene, Quebec Provincial Ministry of Health, who cheerfully undertook all the lead estimations cited, using the dithizone colorimetric method.

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PREMALIGNANT FIBROEPITHELIAL TUMOUR OF PINKUS

R. JACKSON, M.D.* and J. D. STEPHEN,† M.D.,
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PREMALIGNANT fibroepithelial tumour of Pinkus is a rare neoplasm usually occurring in the skin of the lumbo-sacral area and having a specific histological picture. It was first described by Pinkus[5] (1953), who reported four cases. Nine other cases have been reported by Degos and Hewitt[1] (1955), Gertler[3] (1955), Venkei and Sugar[6] (1956), Gartmann[2] (1956), and Jaeger and Delacrétaz[4] (1956).

The lesions vary in size from 2 mm. to 2 cm., are frequently polypoid, and are of fleshy pink or reddish colour. They have a soft consistence and a smooth surface. The lumbo-sacral area is by far the most common site and the lesions are frequently multiple. Resemblance to seborrhœic keratosis is marked, although there is no follicular plugging and the lesions are not greasy. Adjacent or intermingled lesions have included seborrhœic keratosis, various types of basal cell carcinoma, intraepidermal squamous cell carcinoma and invasive squamous cell carcinoma.

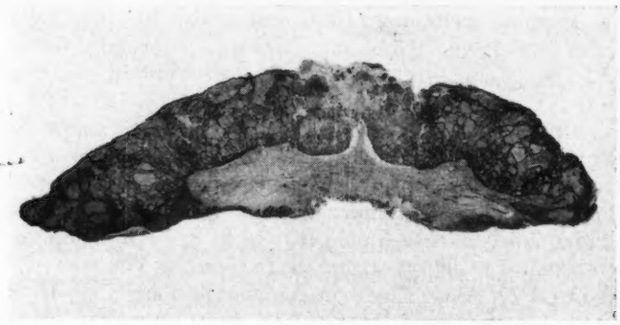

Fig. 1. (Case 1).—Note polypoid shape. All the sections reproduced here have been stained with hæmatoxylin and eosin. × 4½.

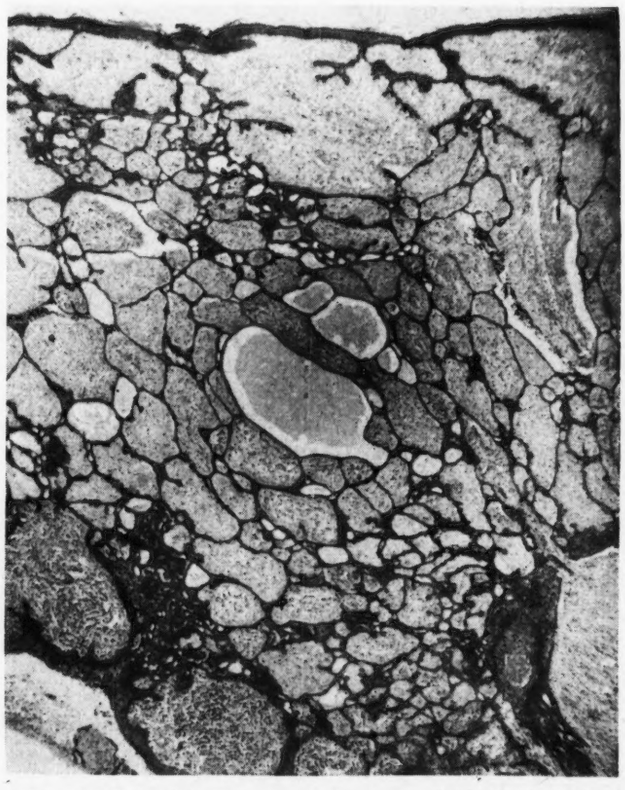

Fig. 2. (Case 1).—Shows lace-like appearance with cystic spaces. × 34.

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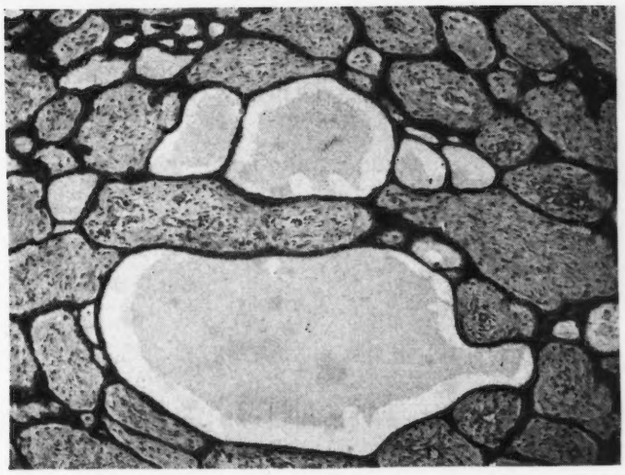

Fig. 3. (Case 1).—Note cystic spaces, branching epithelial strands and islands of connective tissue. × 100.

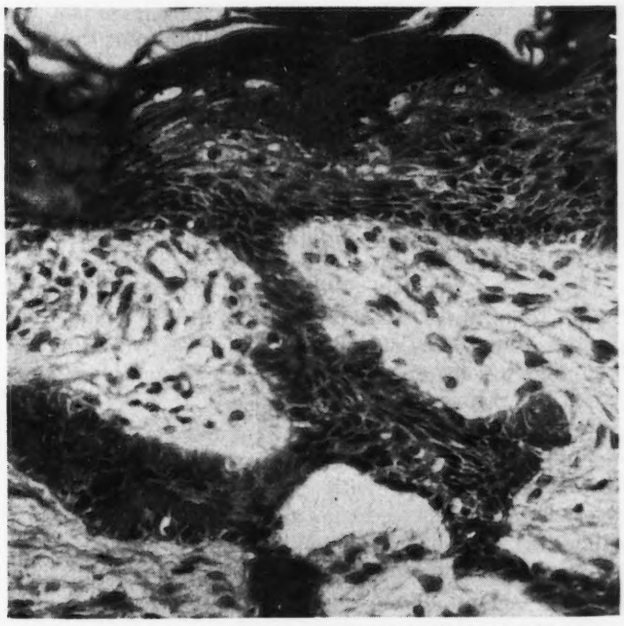

Fig. 4. (Case 1).—Shows small flask-like protuberances ("buds") arising from epithelial strands, also one small cystic space. Overlying epidermis at top. × 400.

Fig. 5. (Case 1).—Note horn cyst. Typical reticulated pattern at upper right and lower right. × 75.

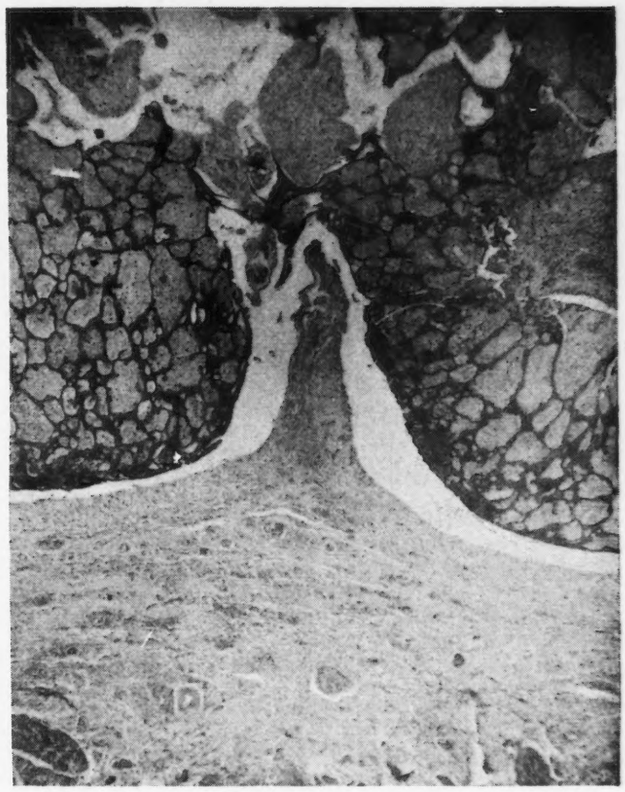

Fig. 6. (Case 1).—Shows slit-like area where underlying corium has separated from the tumour. × 32.

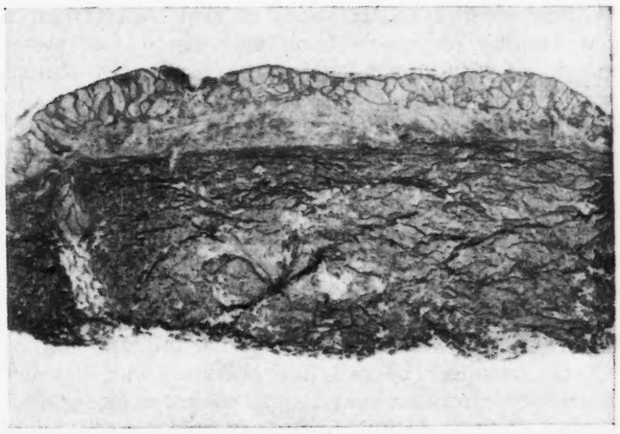

Fig. 7. (Case 2).—Overall view. Note increase in thickness of pale-staining sub-papillary corium. × 10.

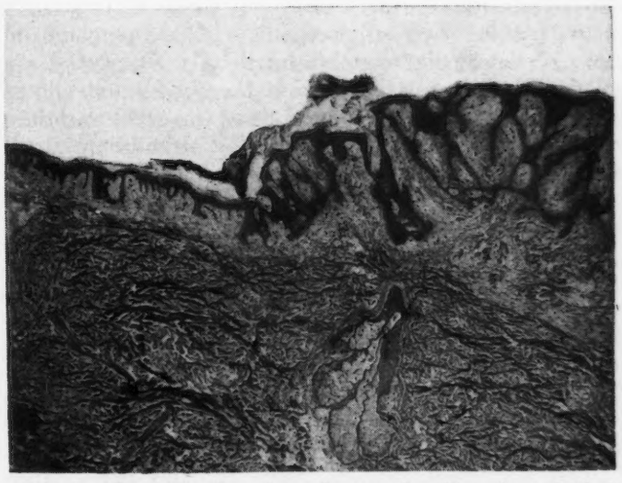

Fig. 8. (Case 2).—Junction of normal epidermis and that of the tumour. × 27.

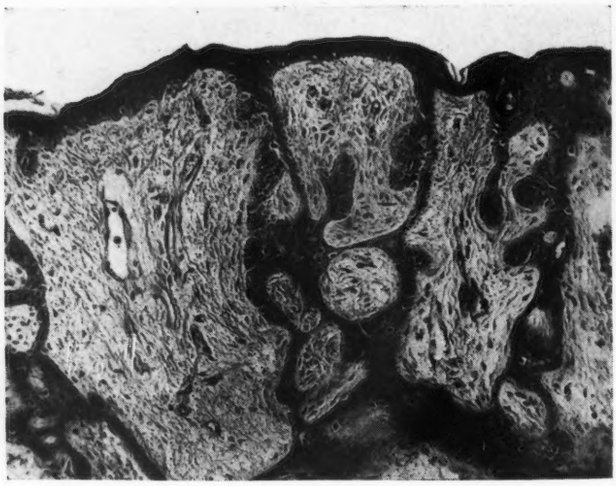

Fig. 9. (Case 2).—Shows lace-like pattern with numerous small epithelial buds. × 140.

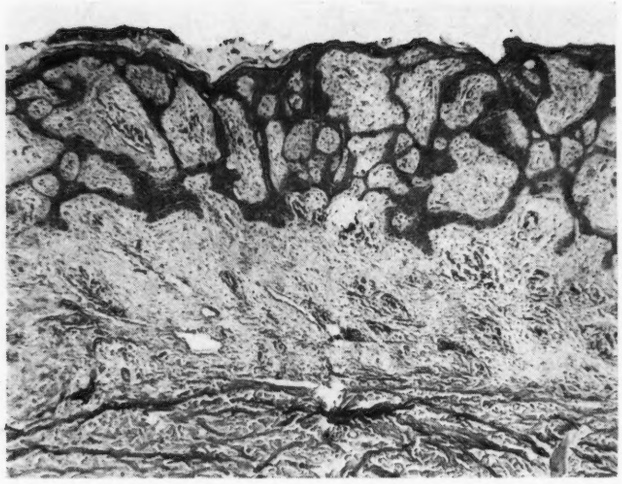

Fig. 10. (Case 2).—Note hypertrophy of sub-papillary corium beneath tumour. × 48.

CASE 1

Clinical findings: The biopsy was taken from the buttock of a 49-year-old male. The tumour had been present for one year. No further clinical information is available.

Pathological Findings

Gross: The specimen consists of a nodular piece of tissue measuring 2 cm. in diameter. This is white in colour and firm in consistence.

Microscopic: The section is of skin. Apart from a few bundles of muscle fibres and one dilated sweat gland, no skin appendages are present. No normal skin is included (Figs. 1 to 6).

The lesion is a polypoidal tumour composed of strands and clumps of epithelial cells. Between most of these strands are bundles of fibrous tissue; between a few are cystic spaces containing a light staining eosinophilic hæmatogenous material. The overall picture is lace-like. The strands of epithelial cells are connected with the overlying epidermis in many places. These strands are two to three cells thick with numerous fusiform swellings especially at the junction of several strands. The cells are cuboidal with a small amount of cytoplasm and a large round or egg-shaped nucleus with a distinct nuclear membrane and fairly coarse chromatin strands throughout. There are occasional large masses of chromatin. Mitoses are rare. No intercellular bridges are seen in sections stained with H. & E. or phosphotungstic acid. Morphologically most of these cells resemble basal cells, although some of the centrally placed cells in the fusiform swellings resemble cells of the malpighian layer. Protruding in many areas from these epithelial strands are small flask-shaped accumulations of similar basal-type cells. These are very similar to the flask-shaped structures seen in multiple superficial epitheliomatosis. Marked peripheral palisade formation is present about some of the "flasks", about some of the larger clumps of epithelial cells, and along almost all of the deep borders of the tumour. On the deeper aspect of the tumour there are long, slit-like, empty areas where the underlying corium has separated from the tumour. These spaces are similar to those seen in many basal cell carcinomas.

The intervening fibrous tissue contains many large fibroblasts and numerous fine collagen fibres. A few small blood vessels and capillaries are present in some of the fibrous tissue islands. Also, in many, there are ovoid accumulations of a homogeneous eosinophilic material. This is presumably degenerating collagen. It is not present about the blood vessels. This material stains a faint purple with the periodic acid Schiff stain and does not stain with Congo red.

The cystic spaces mentioned above are of various sizes, some large, others minute. They are present in the centre of some of the clumps of epithelial cells. Some are empty. In certain areas a cystic space is present at the side of a fibrous tissue area. It may be that all these cyst-like spaces represent areas from which the connective tissue is absent.

The epidermis overlying the tumour has two small ulcers, each with a pyogenic crust and adjacent inflammatory response with polymorphonuclear leukocytes, lymphocytes, œdema, and blood vessel dilation. Otherwise the overlying epidermis is normal. The underlying corium shows numerous dilated capillaries, some of which contain red blood cells.

No pigment is present. There is no typical pattern of basal cell carcinoma. One large typical horn cyst is present.

Diagnosis: Premalignant fibroepithelial tumour of Pinkus.

CASE 2

Clinical Findings

The patient was a 59-year-old man who had had the lesion for many years. No further clinical information is available.

Pathological Findings

Gross: The specimen consists of an ellipse of skin and subcutaneous tissue measuring 2 × 1.4 × 0.2 cm. The centre of the epidermal surface is occupied by a flat, slightly granular, light brown pigmented growth.

Microscopic: This section is of hair-bearing skin (Figs. 7 to 10). The basic histopathological findings are the same as those seen in Case 1. A few minor variations are present. This lesion is smaller and much less developed. There are no cystic spaces. There are no horn cysts. There is a definite hypertrophy of the papillary layer of the corium. In addition to being

present within the tumour, it also is present beneath the tumour and forms about one-quarter of the thickness of the corium.

The change from normal adjacent epidermis and corium to the tumour is abrupt. A few of the basal layer cells contain fine brown pigment granules, even in the tumour itself.

Diagnosis: Premalignant fibroepithelial tumour of Pinkus.

COMMENTS

With a few minor variations, these tumours are the same as those described by Pinkus and others. In Case 1 a single true horn cyst was present. The number and size of the cystic spaces are greater than previously reported. The epithelial downgrowths are composed almost entirely of basal type cells; even those which look like malpighian layer cells do not have intercellular bridges. The cells forming the basal cell buds are not readily separated from the cells forming the lacework. The small areas of degenerating collagen have not been mentioned before.

In Case 2 intercellular bridges were easily found in some of the central cells of the epidermal downgrowths. The hypertrophy of papillary collagen not invaded by the tumour is noted.

The nosology of this tumour has been fully discussed by Pinkus. Most authors agree that it is a variety of superficial basal cell carcinoma (superficial epitheliomatosis), although of very low grade malignancy. The possibility of these lesions being a form of nævus is mentioned by Degos and Hewitt, as one of their patients had had her lesion since childhood. It is important for two reasons. First, it may be confused clinically and histologically with other benign or malignant skin tumours such as reticulated seborrhœic keratosis or basal cell carcinoma with dense fibrous stroma. Second, a study of the relationship between it and other varieties of basal cell carcinoma may provide some insight into their pathogenesis.

SUMMARY

Two cases of premalignant fibroepithelial tumour of Pinkus have been presented.

We are indebted to Dr. J. W. Whittick, Pathologist, Regina Grey Nuns' Hospital, for permitting us to present the second case.

We are grateful to Mr. H. Wood for the photomicrographs and to Dr. N. Hoffmann for assistance with the translation of the German references.

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THE EYE BANK OF CANADA

The Eye Bank of Canada was established in 1956 by the Canadian Ophthalmological Society and the Canadian National Institute for the Blind. Its main purpose is to keep a constant supply of corneal tissues for doctors who are waiting to do corneal transplants. The Eye Bank has provided cornea for more than 100 of these operations. An estimated 1500 people in Canada require this type of surgery, but the shortage of donor tissue gives little hope that more than a small fraction of that number will realize this chance of better sight.

The Eye Bank has available a donor card, an instruction sheet and a copy of a pamphlet entitled "Miracle in Sight" which tells a little of the work of the Bank. Two thousand people have now signed these consent forms and this is the legal authority for the doctor to remove the eyes at death. When the next-of-kin of a patient who has signed such a form asks that the eyes of their relative be given to the Eye Bank, the physician should telephone the Canadian National Institute for the Blind, collect (by day, HU. 5-8644; at night, HU. 5-9476) and all arrangements will be made for the eyes to be shipped to Toronto.

Instructions are available on "How to send an eye in to the Bank" and on "How to enucleate an eye". All hospitals in Ontario with over 135 beds have been equipped with sterile Eye Bank bottles in which eyes are placed for shipment to the Bank, together with instructions on how to do this. These bottles are supplied, at no charge, by the Canadian National Institute for the Blind.

The co-operation of physicians is urgently needed to enable this program of sight restoration to be effective. All inquiries should be sent to the Eye Bank, Canadian National Institute for the Blind, 929 Bayview Avenue, Toronto 17.

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SCIENCE AND NON-SCIENCE IN MEDICINE

Most of us have assumed in the past that the scientific method was here to stay, and that future investigation in medicine would be based upon its well-tried techniques. But it seems that there are important parts of the world where this assumption can no longer be made with safety. In a pessimistic article about modern medicine in China (and we mean China and not Formosa) Donald Gould describes the intrusion of politics into the field of therapy (*Lancet*, 2: 633, 1958). In the China of today, there are about 70,000 medical practitioners trained in the methods of Western medicine and another 500,000 practitioners of traditional Chinese medicine. The latter practise the ancient techniques of acupuncture (a method of white magic based on insertion of needles into various parts of the body in accordance with symptoms), moxibustion or cupping, and herbal medicine, which is entirely empirical.

Now it is easy to understand that with the frightful shortage of trained physicians the government must for some years lean heavily on the services of the latter. This has nothing to do with politics, and is the system encouraged by public health workers in underdeveloped countries, as in the case of native midwives, who with a little reorientation can do good work. But what depresses Dr. Gould is the fact that a glorification of Chinese traditional medicine is going on with every encouragement from the top, and trained physicians are being made to study the methods of the traditionalists, with the intention that they will eventually be taught in medical schools alongside scientific medicine.

It may be argued that the orthodox can learn a little from the others. Chinese herbal medicine may contain some drugs, like rauwolfia, which can with profit be absorbed into the therapeutic armamentarium of the physician, and it is as well to have some knowledge of the details of unorthodox treatments before condemning them out of hand. But this is apparently not the design of the government. They have set up "research institutes" in acupuncture and in herbal medicine but there is no sign of scientific research as we understand the term, to develop useful drugs for example, and to weed out the magic. Rather the intention is to prove that the methods are sound and that physicians are at fault in having neglected them for so long. We read with surprise that Canada is included among those countries which are asserted to have accepted and adopted acupuncture, though we cannot recall any statement from Ottawa or from the Council of the C.M.A. to this effect. Maybe the Committee on Economics should consider the problem, since we read that "one acupuncture doctor cured 250 patients at a total cost of $12.50. By orthodox treatment, 35 similar patients would cost $339.50 to cure."

The point that worries Dr. Gould is that it seems to him logically impossible to teach the two systems side by side, since a man who believes in the one (science) cannot appreciate the other (non-science). He sees as a consequence that medical advances must cease, and that medicine in China will undergo a period of stagnation like that which obtained for so many centuries in Europe through the dead hand of Galen. The Party will become the only competent authority in medicine as in all else, thus making China a more truly Communist state than Russia, which has never tried to blend folklore with science to any extent. He also sees the ruin of the medical profession as an effective force in the community, and a deliberate attempt to rid the country of a band of men and women trained in habits of critical thought and therefore harmful to the state.

One wonders whether the "working schizophrenia" which Dr. Gould finds logically impossible, namely the practice of scientific medicine and of traditional medicine by the same man, is in fact impossible. Most of us are somewhat schizophrenic in our attitude to science. We find no difficulty in thinking in scientific terms of one part of our life, and maintaining old superstitions and myths about the rest. If this is drawn to our attention, we console ourselves with the thought that medicine is not a science but a mixture of science and art. In fact the number of physicians who carry science into every corner of their lives must be very small—but that is very different from being compelled by edict to believe in nonsense.

Nor do we see any evidence from the Chinese medical literature that the medical profession is in any hurry to glorify traditional medicine at the expense of Western science. It is true that the medical journals carry little notes about quaint figures of traditional medicine, and some material on clinical trials of herbal remedies. But the main body of the journal is usually devoted to scientific articles which cite with approval American work and contain descriptions of research not too different from our own. There may be a little more enthusiasm (perhaps we could copy it with ad-

vantage), as in the first article in the August issue of the *Chinese Medical Journal*, which is entitled "The People's Boundless Energy During the Current Leap Forward. New Victories on the Anti-schistosomiasis Front", but this is very laudable in a country where there is so much to be done in the shortest time possible.

In any case, do we not believe that ultimately "truth by its own sinews will prevail"? Even if some politicians try to prevent it.

Editorial Comments

AORTIC OCCLUSION

Recent advances in the definitive surgical therapy of cardiovascular disease have accented the importance of accurate anatomical diagnosis, not only of purely cardiac anomalies but also of various occlusive diseases of the peripheral arteries. The steps that have already been taken in this direction, especially in connection with the cerebral manifestations of carotid artery disease, are well known to most physicians. Along similar lines, a great deal of interest is now being shown in obstructive disorders of the larger arteries, including the aorta itself. To date, most of the interest has centred itself about the abdominal aorta and its common iliac branches,[1-3] but the problem of thrombo-obliterative disease of branches of the aortic arch[4] has not been neglected.

As might be expected, intermittent claudication is the outstanding complaint in lower aortic occlusion, and both British and American workers consider this to be the most reliable indicator of arterial insufficiency. Intermittent claudication has, of course, been recognized as a clinical entity for many years; its present interest lies in the realization that, contrary to previous opinion, it is not usually the result of widespread narrowing of the lumen of peripheral vessels, but is more commonly due to one or more localized segmental occlusions, secondary to thrombosis of the aorta and common iliac arteries. On this point, British, American and Canadian investigators are all in agreement.

Loss of power in the lower limb muscles with extensive muscle atrophy is probably the next most important finding, but there is disagreement as to its frequency. In a recent British report, it was found in approximately half of 32 patients, while in a contemporary American study, consisting of 207 patients, "extensive atrophy of the muscles of the thigh was occasionally seen, but was not frequent in this series".

A very distressing symptom in aortic occlusion is impotence. Although the frequency of this finding was emphasized by earlier workers in this field, notably Leriche, there is less tendency among more recent investigators to consider it of striking importance. In the first place, later workers have found it to be an uncommon complaint, and its natural history as part of this condition is somewhat confusing because "spontaneous cure of the symptom may occur, and the significance of operation in sometimes relieving it is not yet clear".

Naturally, there are other less common findings associated with this condition, including persistent backache, coldness of the extremities, renal ischæmia and superficial, as well as major, cutaneous ulceration and gangrene. However, so-called "symptomless aortic occlusion" can occur; in most such cases, thrombosis of the abdominal aorta is found at autopsy, having been unsuspected during life. However most, if not all, of these patients have been seriously ill and bedridden for some time before death, and symptoms of aortic occlusion would not be likely to be prominent.

It is most interesting to note that there seems to be complete agreement among Canadian, American and British workers as to the basic etiology of aortic thrombosis, all of these workers implicating atherosclerosis as the fundamental cause. From the standpoint of accurate diagnosis, however, there is agreement in principle, but not in practice, as to the place of aortography in corroborating the diagnosis and delineating the extent and severity of the obstruction. The American and Canadian workers recommend this diagnostic procedure "only in selected cases" and the Canadian workers go so far as to state that translumbar aortography "is not indicated unless surgical measures are to be undertaken". On the other hand, the British workers consider that, if the procedure is carried out under strictly standardized and controlled conditions and with adequate experience, morbidity and complications from this diagnostic aid can be reduced to a minimum. In one British institution, some 500 aortograms have been taken during a four-year period, mainly on patients with arterial disease, and the only significant complication encountered has been a single case of temporary anuria. These workers consider that, provided adequate precautions are taken and the problem of dosage of contrast medium is fully understood, aortography in suspected cases of aortic thrombosis is fully justified.

Thus far we have been concerned with obstructive lesions of the abdominal aorta, particularly in its lower regions, with effects on the circulation to the lower extremities. However, recent work has indicated that segmental thrombo-obliterative disease of the branches of the aortic arch is in itself a clinical entity, resulting in occlusion of one or more of the larger vessels arising therefrom, and characterized by manifestations of ischæmic disturbance and the absence of pulses in the head, neck and upper extremities. In contradistinction to the situation in the lower aorta, the basic etiology is not so well established, various factors having been proposed as contributing to its causation, such as syphilitic aortitis, non-specific arteritis, atherosclerosis, thromboangiitis obliterans, trauma, "allergic reactions", and specific infections.

Whatever the basic causation of obliterative aortic disease in both sites may be, the underlying problems remain the same, namely, diagnosis of the existence of aortic obstruction, determination of its extent, and finally treatment. The first two have already been discussed. As to the latter, recognition of the existence of these clinical syndromes and their treatment have gone hand in hand. One must

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accord high praise to the surgeons for the invaluable part that they have played in both these aspects of the problem, since it must be freely admitted that medical measures in these occlusive diseases of the larger branches of the vascular tree have been of no practical value. It has been to a great extent the surgeons who have stressed the localized character of aortic occlusions, thus leading the way to a reasonable approach to treatment which takes advantage of this segmental distribution. So much is this the case at present that it is now quite common practice for vascular surgeons to insert "replacement" or "bypass" grafts to improve the circulation in these large arteries, or even to return it to a completely normal state. It would appear from the published literature that graft material from artery banks and synthetic plastic tube material are equally acceptable.

Finally, it is of some importance to take a long view of the situation and it should be pointed out that British workers feel that "aortic thrombosis is neither rare, nor, in most cases as dangerous to life as was previously thought". They point out that the assessment of the long-term results of vascular surgery in occlusive aortic disease is not yet possible, and that the dangers of major surgery in these patients, who are often very poor surgical risks, must be carefully weighed against the prognosis of the untreated disease. The experience of some workers, particularly those in England, has indicated that the prognosis is much less gloomy than has been generally believed. S. J. SHANE

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AN ENCOURAGING REPORT*

An interesting report has recently been published by the New York State Joint Legislative Committee on Mental Retardation. It is an account of what the Committee has been able to accomplish legislatively since it was formed in late 1955, together with its proposals for the future and the advances made by the Education Department, the Department of Mental Hygiene, the Interdepartmental Health Resources Board, and private organizations. This is indeed an impressive document. The Committee can point with justifiable pride to the progress made as the result of more than 35 bills of which it has been the main sponsor.

The Education Department, for example, is now required to maintain a register of mentally retarded children, just as it has hitherto done for the physically handicapped. Boards of education must set up appropriate classes and facilities for the care and education of mental retardates between the ages of 5 and 21. In addition, small classes of mentally handicapped children may now receive the same amount of financial aid as a regular elementary school class with an average daily attendance of 25 pupils.

The Department of Mental Hygiene announces the very considerable expansion of its educational program, which has kept pace with the facilities provided for children in community schools, and it expresses the firm belief that the schools of the State institutions have an important future role. Aftercare services have been expanded in recent years and four aftercare clinics, staffed by full-time psychiatrists and psychiatric social workers, serve different boroughs of New York City. Then not content with one internationally known research unit at Letchworth village, under Dr. George A. Jervis, the Department is organizing a second research unit at Willowbrook State School and has already appointed a director of research to head it. This step is thought to presage a substantial increase in the already considerable volume of research in mental retardation carried out within the Department.

It is however within the province of the Interdepartmental Health Resources Board that the most striking innovation is to be found. Apart from providing the main support for three mental retardation clinics and publishing a number of valuable and important research projects, the Board is currently responsible for organizing two demonstration community centres, one in the city of New York and one in the central part of the State. Although the primary purposes of demonstration community centres are set down in the description of the law authorizing them as case finding, comprehensive differential diagnosis and parent counselling, such centres actually represent a far more ambitious scheme than the ordinary mental deficiency clinic. The very wide range of their activities is admirably summarized later in the report. Thus their objectives are threefold: (1) To provide suitable services for all mentally retarded children and adults who are not in institutions or public school classes. (2) To determine the effectiveness of such services in developing their full potentialities in social adjustment and economic usefulness. (3) To determine the role and responsibilities of the State, local government and private organizations in providing such services as prove effective. Those to be served are pre-school children, school age children rejected by schools as "uneducable", custodial children kept at home by parents, severely retarded adults at home, children 16-21 years of age, and parents needing counselling services.

Their comprehensive nature can perhaps be best appreciated from the description of the types of service offered. The list is certainly imposing. Day training centres exist for pre-school and school age severely retarded to further self-help, communications, and group participation. Sheltered workshop and vocational guidance units are provided for severely retarded adults and educable mentally retarded children who have left public school classes. There is a recreational centre for adolescents and adults to provide social activities, and a placement service for those benefiting from sheltered workshop or vocational training activities, as well as a counselling service for parents of

*Report of New York State Joint Legislative Committee on Mental Retardation, Legislative Document 1958, No. 83.

mentally retardates, to further their understanding of the problem and how best it may be met. A "half-way" house or residential unit for those coming out of State schools, and those on waiting lists for re-entrance, prepares both child and parents for his return to the community or for leaving home.

This encouraging report can be seen as yet another indication of the constructive efforts being made at all levels to tackle the problems of mental retardation.

ROBERT GIBSON

ADOLESCENT MEDICINE—A NEW SPECIALTY?

Advances in medicine are achieved not only through ever increasing knowledge but also through regrouping and reorienting of knowledge already available. The historic division between physicians and surgeons, although still present, is being replaced by specialization based on regions or groups of diseases on the one hand (such as cardiology or urology), and age groups on the other hand (such as pædiatrics and, more recently, geriatrics). There are obvious advantages in reorientation when the concerted efforts of physicians and surgeons, physiologists and pathologists, psychiatrists and biochemists are all focused on one particular group of problems. Even if such specialization may at times be temporary, it is important that medicine should have shown itself capable of responding to the needs of time in marshalling the forces required to solve specific problems.

Biehusen[1] claims that adolescents have received less attention from medicine than any other age group. As an in-between group they do not fit into pædiatrics, nor is internal medicine concerned with them. There is need for more knowledge of their problems and until recently there were no postgraduate courses in "adolescent medicine" available. Only a few clinics for adolescents exist in the United States, and the author describes the common problems of the adolescent as he encountered them in such a clinic at the Letterman Army Hospital in San Francisco.

From the adolescent unit of the Children's Hospital in Boston (which has obviously influenced the author) comes a series of articles reporting recent contributions to the literature on adolescent medicine. For example Gallagher (director of the Adolescent Unit), Heald, and Masland[2] review the various articles pertaining to such conditions as pancreatitis, thyroid disorders, and ulcerative colitis, all encountered in adolescents. It goes without saying that acne, menstrual disorders and leukorrhœa receive special attention. A study of 6000 school-children indicates that visual testing should be continued through the high school years, because twelfth-grade pupils show marked deterioration of vision as compared with the younger children.

The review points to the help which physicians can obtain from a recently revised book by Phelps, Kiphuth, and Goff on the diagnosis and treatment of postural defects, so common and yet so often neglected a field. These defects are most easily remedied in the adolescent, and correction can have far-reaching results in improving both mind and body. Motor co-ordination rapidly improves during adolescence, and awkwardness may be an expression of a lack of savoir-faire, fear or unhappiness, or of the fatigue that accompanies very rapid growth.

Much sound advice which applies to good medical practice in general and to adolescent medicine in particular can be obtained from a perusal of these papers. They stress the need for the establishment of adolescent clinics, and the authors recommend that consultations with other specialists should be restricted to an absolute minimum. When consultations become necessary the consultant should, if possible, come to the patient in the office of the clinic physician, so as not to weaken the patient-physician relationship. Whether adolescent medicine will emerge as a new specialty remains to be seen. The emotional problems and some of the physical problems of this age group are fairly well known, or so it seems. More knowledge in this field is undoubtedly desirable, and postgraduate courses in adolescent units not necessarily attached to children's hospital may be one answer.

W.G.

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NATIONAL HEALTH SERVICE IN THE UNITED KINGDOM

According to the annual report for 1957 of the Ministry of Health, the cost of the National Health Service in England and Wales rose to a new high level last year of 1638 million dollars.* This was 140 million dollars more than in the previous year. Four-fifths of this total cost came from the Exchequer, showing what a tremendous burden the service must be upon the taxpayers. As a matter of fact, less than 100 million dollars came from charge to patients at the time of receiving service.

The national drug bill rose to a record 169 million dollars, or nearly 10% of the total cost of the service. There were 207,209,397 prescriptions issued by the 15,856 chemists identified with the scheme. The increased cost is said to be due to the average prescription's rising in price to five shillings and ten pence (77c) against a price of 42c in the year 1949. More than 50% of the prescriptions were for proprietary medicines, and they accounted for 74% of the total drug ingredients prescribed. Antibiotics were the biggest item at 19.94%. Next came the hormones, which were 9.72%.

The hospital and specialist outlay rose by more than 80 million dollars to 936 million dollars—between 55 and 60% of the total cost. The waiting period for hospitalization has apparently not improved, as at the end of the year 9000 more patients were awaiting admission than the year earlier. Although 29% more were dealt with than in 1949

*Canadian rate of $2.50-$2.75 to the £1. 0s. 0d.

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in hospital, there were only about 6% more beds than at the start of the service ten years ago. More than 12 million new patients were treated in the out-patient departments, as compared to 1956. The number of patients entering mental hospitals has been rising steadily for many years. Despite warnings of dangers, the demand in hospitals for radiological services continued to increase.

In a foreword to the report Mr. Walker-Smith, Minister of Health, says that no Minister or government could do all that was needed for the people in this field, and therefore priorities must be settled wisely. To quote him—"Resources must be used with maximum efficiency to the best advantage. Success depends on understanding and co-operation on the part, not only of all concerned in the running of the service, professional and lay alike, but also of the patients. The achievements of the National Health Service in its first decade, in circumstances which have never been easy, have been substantial, and should be recognized as such."

By and large, the people of the United Kingdom will in greater majority say that the service has been a success. The point of view of the medical profession is indeed a mixed one. Many feel that the working conditions, and especially the remuneration of the family physician, have left much to be desired. However, the British Medical Association is keeping a constant close eye on the whole scheme, and they hope that it may ultimately emerge as a satisfactory health service for both the people who receive the services and the professions who provide them.

ANOREXIA NERVOSA: A SOMATIC DISORDER

Is anorexia nervosa to be regarded as a somatic or a psychiatric disorder? Taking the standpoint that the somatic element is dominant Williams has recently reviewed the cases of 53 women admitted to the London Hospital with the diagnosis of anorexia nervosa since 1897 (*Brit. M. J.*, 2: 190, 1958). In this group 46 patients who did not receive tube feeding had a total of 57 admissions, of which 46 were considered therapeutic failures. On the other hand seven patients were given tube feeding with very gratifying immediate results. There was considerable gain in weight with both physical and mental improvement. The writer recalls the various methods of treatment of anorexia nervosa since Sir William Gull originally described it in 1874, and takes issue with the regimens which do not include tube feeding. He found that the results of treatment even with tube feeding are largely of temporary value; recovery, if it takes place, is apparently spontaneous. "Only a few when questioned in retrospect could give a precise reason for recovery, and in these it was often as whimsical as the circumstances which had first precipitated the illness." Williams points out that psychiatrists are almost unanimous in insisting that psychotherapy is the treatment of choice, and that some of them advocate that no attention should be paid to the problem of nutrition and no reference made to diet. Since psychiatry has not been any more successful than medicine in curing large numbers of these patients, Williams concludes that the treatment should be somatic because the main features of the disease are somatic. He cites Hurst, who in 1939 reported the results of his treatment based on the same principles as those described by Ryle and by Ross a few years earlier. They treated their anorexic patients with explanation, firmness and good temper, and found that even the most resistant patient could then be persuaded to consume a good meal, after which her progress was uninterrupted. Williams believes that the majority of cases which responded to such a treatment were mild; of the 46 patients reported by Ryle to have been successfully treated by this method 11 had no amenorrhœa, thus not fulfilling the criteria for the diagnosis of anorexia nervosa.

There are several controversial points in this otherwise very instructive paper. First of all, it is doubtful whether the presence of amenorrhœa is a *sine qua non* for the diagnosis of anorexia nervosa. Furthermore the name of this disorder implies that its origin is emotional and not organic, and anyone who has watched a patient develop the full-blown picture of anorexia nervosa from its earliest beginnings must be convinced that the cause is to be found in a disordered mind. It goes without saying that its somatic results are serious and can be fatal, but these are obviously consequences of undernutrition. Whether it should be classified with the neuroses or psychoses may depend on the prevailing trends in psychiatry, but psychiatrists are the first to admit that chronic neurosis is at least as resistant to therapy as most psychoses. Failure of psychotherapy is not sufficient reason for excluding this disorder from the list of psychiatric diseases. However, one can heartily agree with Williams that these patients are primarily the physician's responsibility and should be treated by him. In most cases which resist treatment by medical means, as outlined by Hurst and including intubation if the physical condition of the patient demands it, the advice and help of a psychiatrist can be of very great value. One should not underestimate the iatrogenic component in the patient's resistance to therapy. The physician who in the earlier stages of the disease was not sure of the diagnosis, and who very properly tried to exclude all the possible wasting diseases including endocrine disorders, may have planted the seeds of doubt in the patient's mind that an organic cause will eventually be found, and that it is not up to the patient to make the effort. Psychotherapy may help to remove these doubts and thus pave the way for better co-operation on the part of the patient.

Failure of others to reproduce the results obtained by Ryle, Ross, and Hurst is not necessarily an argument against their method of treatment; could this rather not be a sad commentary on the state of the art of healing as practised by our present generation of physicians? W. GROBIN

Medical News in brief

ALLERGY TO PENICILLIN IN POLIOMYELITIS VACCINE

Six patients developed skin reactions after injection of poliomyelitis vaccine (Zimmerman: *J. A. M. A.*, 167: 1807, 1958). In some of them a known allergy to penicillin existed, and in all of them the vaccine given contained small amounts of penicillin. Administration of penicillinase cleared the urticaria promptly without any other treatment and without recurrence. Giving a vaccine which contained penicillin to one of the patients together with penicillinase failed to reproduce the reaction. Vaccine which was free of penicillin was subsequently given to other patients and it did not produce any reactions. The author considers these observations as proof that in his cases and probably in many others the penicillin contained in poliomyelitis vaccine was responsible for skin reactions.

MEPROBAMATE IN PSYCHIATRY

In Finland, a comparison was made between meprobamate and chlorpromazine treatment in 158 patients (128 psychoneurotics and 30 schizophrenics.) In reporting his studies (*Ann. med. int. Fenniæ*, 47: 47, 1958) Hormia confirms the poverty of effects of meprobamate in schizophrenia, when given in doses of 400 to 800 mg. four times a day. On the other hand, in the psychoneuroses the results were better than with chlorpromazine, and the action of the drug began more rapidly, while somatic side effects were less. Best results were achieved in acute anxiety states. In chronic cases, the effect of meprobamate sometimes diminished during the course of treatment; in such cases a combination of meprobamate with chlorpromazine proved effective. Meprobamate was also thought to be useful in preventing the onset of parkinsonian symptoms during treatment of schizophrenia with chlorpromazine. Meprobamate was considered effective in preventing relapse in psychoneuroses.

BLEEDING DUODENAL ULCER WITH AND WITHOUT SURGERY

Of 1149 clinical records having diagnoses including duodenal ulcer with hæmorrhage or gastro-intestinal hæmorrhage, 142 were selected by Donaldson, Jr., Handy and Papper (*New England J. Med.*, 259: 201, 1958) for study because each of these contained reliable evidence of significant gastro-intestinal bleeding and duodenal ulceration. Six of these cases were lost to follow-up study and thus the present report deals with 136 patients admitted to a Veterans Administration hospital in the period January 1947 to December 1952. Their ages varied from 20 to 79, and all but one were males.

Of the 100 patients who were admitted with the initial hæmorrhage, there are 37 survivors who five years later had neither recurrent hæmorrhage nor gastrectomy, but 38 had recurrent hæmorrhage (10 of these on more than on one occasion). Eleven of the patients died within the five-year period, eight of these over 50 years of age because of uncontrolled hæmorrhage. Another group of 36 patients gave a history of one or more episodes of bleeding before their first admission and 15 of them had further hæmorrhages during the next five years. There were no deaths in this group during the five-year follow-up; 23 had had gastrectomy and 13 remained free of hæmorrhage and did not have any operations. The authors emphasize the seriousness of bleeding by pointing to the fact that only one-third of the patients in this series escaped subtotal gastrectomy, recurrent hæmorrhage or death. Ten of the 48 patients who had gastrectomy primarily because of bleeding experienced recurrence of hæmorrhage within five years of operation and one other has had a bleeding episode more than five years after surgery.

COMPLICATIONS OF STEROID THERAPY

In Nottingham, England (Morton: *Proc. Roy. Soc. Med.*, 51: 317, 1958), a study was undertaken on the incidence of and the reasons for peptic ulceration during steroid therapy. Dyspepsia is common during steroid therapy and must be differentiated from proven peptic ulceration.

There appears to be a slightly higher incidence of peptic ulcer in patients with rheumatoid arthritis not receiving steroid therapy than in the general population. This may be due to aspirin or phenylbutazone therapy or to the disease itself. A table compiled from the literature and the author's own series show that peptic ulceration with symptoms occurs in a greater number of patients receiving steroid therapy than in a control group. Injected corticotrophin is less likely to produce ulcer than the orally administered steroids, and the author suggests that at least some of the ulcerogenic action may be due to local action of concentrated steroid on the gastric mucosa. Attempts to administer steroids in enteric-coated tablets in order to prevent this local action have not been successful in the author's hands, as absorption was unreliable.

PATHOLOGY OF DEATHS DURING INFLUENZA EPIDEMICS

A paper from Melbourne, Australia (Bowden and French: *M. J. Australia*, 1: 553, 1958), records observation on 13 virologically proven cases of influenza in which post-mortem examination was carried out. Two of these patients died during the epidemic of 1950, two during the epidemic of 1956, and nine during the 1957 epidemic of Asian influenza in Melbourne. Five of these persons were infants, two were young adults, and six were elderly people with varying degrees of coronary arterial heart disease.

Histological examination revealed marked hyperæmia of the tunica propria of the bronchial tree and infiltration of the tunica propria and sometimes of the epithelium with inflammatory cells, among which plasma cells were often conspicuous. There was degeneration of the epithelium of the mucous and serous secreting glands, with plasma cells often predominating about these damaged glands. Toxic myocarditis may have been important in the elderly as a cause of death whilst associated bacterial infection may have been fatal in the infants.

(Continued on advertising page 54)

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MEDICAL FILMS

CONTINUING the listing of available films on medical and related subjects, we list below additional films. The films are held in the National Medical and Biological Film Library and are distributed by the Canadian Film Institute, 142 Sparks Street, Ottawa, Ontario. The evaluations have been prepared by Canadian specialists in the subjects of the films, under the Medical Committee of the Scientific Division of the Canadian Film Institute, which is headed by Dr. G. H. Ettinger.

OBSTETRICS AND GYNÆCOLOGY

Laparotrachelotomy (Low Cervical Cesarean Section)—1930-36; Sound; B & W; 69 minutes.

Produced by the late Joseph B. DeLee, M.D., Chicago Lying-In Hospital.

Description.—An instructional-training film, demonstrating the procedure and technique of low cervical Cæsarean section.

Appraisal (1945).—A very fine film, thoroughly treated and clearly presented in every respect; it could hardly be improved upon. Especially good as a teaching aid for senior medical students and for postgraduate instruction of doctors. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library ($7.50). For purchase apply to Sol T. DeLee, M.D., 6909 S. Cregier Avenue, Chicago 49, Illinois.

Manual Rotation in the Management of Occiput Posterior and Occiput Transverse Positions—1943; Silent; Colour; 47 minutes.

Produced by the Visual Medical Education Department, Northwestern University, Chicago, Illinois. Technical Advisers: H. J. Holloway, M.D. and E. S. Burge, M.D., Department of Obstetrics and Gynecology

Description.—An instructional-training film, illustrating a method of manual rotation for cases which fail to rotate anteriorly.

Appraisal (1947).—A good film, clearly presented and exceptionally well explained, but rather long, with a great deal of repetition. Recommended for all medical audiences and for students in the clinical years. Suitable for nurses. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library ($6.00). Purchase from Visual Medical Education Department, Northwestern University, Chicago, Illinois.

Normal Labor at Term (The Physiology and Conduct of Normal Labor)—1931; Silent; B & W; 60 minutes.

Produced by the late Joseph B. DeLee, M.D., Chicago Lying-In Hospital.

Description.—An instructional film, illustrating the physiology and conduct of normal labour.

Appraisal (1945).—Two separate groups appraised this film. One group was unanimous in thinking it was most excellent, fully up to date, clearly presented and easy to understand; all were in favour of this type of film. The other group felt some points of technique were confused, that it was generally up to date but with some points open to criticism, and that unassisted labour, now a rare occurrence in medical teaching, should not be shown in an instructional film. Film's audience level is senior medical students, interns, physicians and nurses. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library ($6.00). For purchase apply to Sol T. DeLee, M.D., 6909 S. Cregier Avenue, Chicago 49, Illinois.

Obstetrical Maneuvers on the Ayers Manikin—1943; Sound; Colour; 22 minutes.

Produced by Dr. H. E. Ayers and Dr. J. G. Mussio, Department of Obstetrics and Gynecology, New York Medical College.

Description.—An instructional-training film, demonstrating the value and uses of the manikin in the teaching of obstetrics.

Appraisal (1945).—A fine demonstration of the multiple uses of the manikin in obstetrical teaching, notably forceps and x-ray pelvimetry. Modern in every way and recommended for senior medical students, interns, general practitioners and obstetricians. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library ($4.00). For purchase apply to the Clay-Adams Company Inc., 44 East 23rd Street, New York 10, N.Y.

Primary Dysmenorrhea—1947, revised 1950; Silent; Colour; 44 minutes.

Produced by the Medical Service Department, G. D. Searle & Company.

Description.—An instructional-record film, presenting some of the problems of diagnosis and treatment of primary dysmenorrhœa.

Appraisal (1951).—A clear and accurate presentation, except that it describes too much of the technical investigation and not enough of the clinical. Most interesting to clinicians interested in gynæcology and to technicians doing laboratory investigations. Students should also be interested; there are very few instructional sequences, but showing of the film should be encouraged even though lacking in some respects. Recommended for specialists in gynæcology, general practitioners and medical students in the clinical years. Suitable for medical technicians. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library ($4.50). For purchase apply to Medical Service Department, G. D. Searle & Company, P.O. Box 5110, Chicago 80, Illinois.

Simplified Obstetrical Care—1948; Sound; Colour; 43 minutes.

Produced by the Department of Medical Art and Visual Education, Southwestern Medical College, Dallas, Texas.

Description.—An instructional-training film, illustrating simplified procedures for the care of the obstetrical patient from the time of admission to the labour room until discharge from hospital.

Appraisal (1950).—A straightforward exposition of what the authors desired to present. The theme is worth while, and the techniques employed are effective. Audiences should be benefited by the film. It is recommended for medical students in the clinical years, interns and nurses, and is suitable for general practitioners and other medical audiences. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library ($8.00). Purchase from Medical Illustration Service, 3605 Cedar Springs Avenue, Dallas, Texas.

Standard Obstetrical Routine—1937; Silent; B & W; 61 minutes.

Produced by the Rodney Gilliam Company, Hollywood, Calif.

Description.—An instructional film, illustrating the obstetrical routine and the care of the newborn, as practised in the Los Angeles County Hospital.

Appraisal (1945).—Recommended for medical students, interns, nurses and general practitioners. A good film, although somewhat too long. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (free loan, courtesy of the Mennen Company Limited). For purchase apply to the Mennen Company Limited, 64-66 Gerrard St. East, Toronto, Ont.

Technique for Tubal Sterilization—1944; Silent; Colour; 10 minutes.

Produced by Willard R. Cooke, M.D., Department of Obstetrics and Gynecology, University of Texas.

Description.—An instructional-record film, illustrating a surgical technique for tubal ligation.

Appraisal (1947).—Short, concise, well described and demonstrated, and to the point. Recommended most definitely for specialists in gynæcology and for all other interested medical audiences. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library ($2.00). For purchase apply to Willard R. Cooke, M.D., Department of Obstetrics and Gynecology, University of Texas, Galveston, Texas.

The Treatment of Breech Presentation—1932; Silent; B & W; 64 minutes.

Produced by the late Joseph B. DeLee, M.D., Chicago Lying-In Hospital.

Description.—An instructional film, illustrating methods of delivery in breech presentation, diagnosis and treatment.

Appraisal (1945).—Extremely well presented; most modern; extensive in its description of types encountered. Highly recommended for senior medical students, interns, general practitioners, and specialists in obstetrics. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library ($6.00). For purchase apply to Sol T. DeLee, M.D., 6909 S. Cregier Avenue, Chicago 49, Illinois.

Treatment of Face Presentation—1941; Silent; B & W; 61 minutes.

Produced by the late Joseph B. deLee, M.D., Chicago Lying-In Hospital.

Description.—An instructional film, illustrating the diagnosis and treatment of face presentation.

Appraisal (1945).—A very clear and up-to-date presentation of the subject. Recommended for senior medical students, interns, general practitioners and obstetricians. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library ($6.00). For purchase apply to Sol T. DeLee, M.D., 6909 S. Cregier Avenue, Chicago 49, Illinois.

Trichomonal and Monilial Vaginitis—Pathology, Diagnosis, Treatment—1948-50; Sound; Colour; 17 minutes.

Produced by the Medical Film Guild, New York, for Medical Service Department, G. D. Searle & Company.

Description.—An instructional film, illustrating the pathology, diagnosis and treatment of trichomonal and monilial vaginitis.

Appraisal (1951).—A useful teaching film, clearly presented with good commentary. Recommended for specialists in gynæcology, for general practitioners, for senior medical students, nurses and other medical audiences. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library ($3.00). For purchase apply to Medical Service Department, G. D. Searle & Company, P.O. Box 5110, Chicago 80, Illinois.

TELECAST OF NEUROLOGICAL FILM

Experiments by Canadian doctors on the human senses will be shown on television, November 2, when the Trans-Canada Telephone System's latest Science Series production, "Gateways to the Mind", is telecast over the Canadian Broadcasting Corporation's coast-to-coast network. Experiments, carried out by Dr. Wilder G. Penfield of the Montreal Neurological Institute, form a part of the hour-long film designed to stimulate the interest of young people in scientific careers. Dr. Penfield will explain some of his findings during operations on the temporal lobe.

A film clip of another McGill University experiment shows that man cannot live without sensory stimulation. Volunteers were swathed in soft clothes and placed motionless on comfortable beds in dimly lighted soundproof boxes. No volunteer was able to stick it out more than 48 hours because of the hallucinations suffered.

"Gateways to the Mind" traces man's knowledge of the senses from the time of Aristotle to the present day. After the telecast on November 2, the Trans-Canada Telephone System organizations will make the production available on 16-mm. colour film to schools and other interested groups. Arrangements for hiring the film can be made by calling the local business offices of telephone organizations throughout Canada.

(To be continued)

GENERAL PRACTICE

THE RELIEF OF DEAFNESS BY THE NEWER OPERATIONS*

W. J. McNally, M.D., *Montreal*

Deafness is a family and a community problem in addition to being a personal one. Especially in the very young and the very old, the chief complaints come from the family—concern because the child is not learning to talk or is not doing well in school—or impatience with Grandma because all the gossip has to be repeated for her benefit. Only in isolated incidents does the community assume its responsibility for rehabilitation of the hard-of-hearing.

The ear is our main organ of intercommunication. It is tuned to sound and it has the power of analyzing, sorting out and signalling its presence to the brain for interpretation. If there is excessive noise or sound for too long a time, the ear may be temporarily or even permanently damaged.

History might show that we are living in the noisiest of all ages. Management, labour and the military are beginning to realize the hazards of noise trauma. Noise abatement programs are being introduced, including such measures as the reduction of noise at its source by redesigning machines. Adequate protective mechanisms are being studied for those unavoidably exposed to excessive noise.

Types of Hearing Loss

A hearing loss may be the result of a lesion located in the outer or the middle ear, when it is called a conductive or middle ear deafness. It may also be caused by a lesion located in the internal ear or along the nerves connecting the ear with the brain, and in this latter case it is classed as a perceptive or nerve deafness. Middle ear and nerve deafness may frequently co-exist and complicate the diagnosis.

Nerve Deafness

When the nerve mechanism is damaged from any cause, that is, when there is a nerve or perceptive deafness, the hearing loss is permanent. We have no treatment which will restore the hearing. In many cases efforts to determine the cause of the nerve deafness may be fruitless. One tries to stay progression by safeguarding the patient's general health. There is a great need for research as to etiology and treatment in this large group of patients, probably comprising 50% of all hard-of-hearing people.

Another very unfortunate factor is that it is in this large group that hearing aids may be most unsatisfactory, especially in older patients. Many older people have lost their ability to discriminate between consonant sounds such as "bin" and "tin"—possibly as a result of central nervous system changes. These people are helped by talking more

*From the Department of Otolaryngology, Royal Victoria Hospital, McGill University, Montreal.
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distinctly and directly to them, but are not greatly benefited by mere increase in loudness, which is the main contribution of a hearing aid.

How We Hear

When a sound vibration reaches the ear it causes the ear drum to vibrate. This sets up a movement in the chain of small bones or ossicles which transmit the air vibrations across the middle ear. At the footplate of the stapes in the oval window, the air vibrations are transferred to the fluid in the internal ear. You will remember that the cochlea consists essentially of three closely related coiled tubes. The fluid vibration travels up the scala vestibuli, it cuts across through the ductus cochlearis at the appropriate level, and descends the scala tympani to expend itself against the round window membrane. The round window membrane should always move in an opposite direction to the footplate of the stapes. This must happen because all the other walls of the internal ear are rigid. When the stapes moves in, the round window must bulge outward because the fluid itself is incompressible. This is what is called the phase difference between the oval and the round windows, and it is essential for normal hearing. In the normal ear the intact drum membrane shields the round window membrane from the sound, while it carries the sound directly to the stapes footplate and the oval window.

When a part of the cochlea is activated by a sound-induced fluid wave, a nerve impulse is sent off to the auditory cortex in the temporal lobe of the brain.

In the case of a large open drum perforation, the sound waves may reach the round window membrane and the stapes footplate in the oval window simultaneously. This results in an insufficient phase difference and the cochlea is not properly stimulated.

The operations included under the terms tympanoplasty, fenestration and stapes mobilization, which will be discussed, are attempts to re-establish the phase difference in the internal ear.

Middle Ear Deafness

In the group of patients suffering from middle ear deafness two common causes are, firstly, recurring or chronic middle ear suppuration and, secondly, the condition called otosclerosis in which the joint between the stapes footplate and the oval window develops a bony ankylosis.

Antibiotics have been a great boon to otolaryngology, just as they have been to many other specialties in medicine. With their advent there was the usual over-optimism that some diseases would be abolished. With a greater knowledge of their advantages and limitations, whole new fields of surgery have been opened up which were previously forbidden territories.

In the pre-antibiotic days, surgery for chronic ear infection was destructive, in that frequently structures essential to hearing had to be sacrificed in order to eliminate disease which led to serious intracranial complications, such as lateral sinus thrombosis or brain abscess. These complications may still occur if the antibiotics are used unwisely and if surgery is withheld or not skilfully employed.

Tympanoplasty

With the advent of antibiotics it has been found that in many instances the infection in a chronic ear can be brought under control without operation or with a less destructive type of operation. Structures essential to hearing may be preserved or even reconstructed. As already pointed out, the phase difference between the two windows in the internal ear is essential for good hearing. With this in mind, two German otologists, Zollner (1951) and Wullstein (1952), have devised a group of procedures under the term "tympanoplasty". These are really efforts to carry out plastic operations on the middle ear after infection and suppuration have been thoroughly eradicated and controlled, in those cases in which the nerve or perceptive mechanism of hearing is intact. One cannot overemphasize the primary importance of control of the infection. Depending upon the location of the destruction in the individual case, there is an endless variety of possibilities for surgery. However, for simplicity we shall refer to only two classifications.

The first group of cases are those in which the ossicles have been wholly or in part spared by the disease. There are tests which will show the intactness of the ossicular chain, even though there is evidence of damage involving the ear drum and the middle ear. When all infection has been eradicated, usually by a first-stage operation, a second-stage operation is carried out, at which time a full thickness skin graft can be so placed as to re-establish the integrity of the middle ear. In this way the round window membrane is shielded from the incoming sound. The ossicular chain being intact, the sound is carried through it to the oval window. As a rule in this type of patient the hearing is definitely improved after such an operation.

In the second group of cases the ossicular chain has been damaged beyond repair. The techniques consist of skin grafting to re-establish a modified middle ear cavity which connects the round window membrane niche with the Eustachian tube area. The round window membrane is shielded from the incoming sounds. On the other hand, the stapes footplate is left uncovered and is exposed to the incoming sounds. This re-establishes a phase difference between the two windows.

This is micro-surgery which depends for its success upon good surgical judgment and a sound knowledge of the physiology of the ear. It can only be done properly under the high magnification afforded by the operating microscope. The treatment of chronic suppurative ear disease has been revolutionized and has resulted in the rehabilitation of many persons who were seriously handicapped by hearing loss.

Fenestration

Non-suppurative middle ear disease has benefited from two operations in recent years. The fenestration or window operation for the treatment of cases of otosclerosis was perfected by Lempert in 1939. It is designed to substitute, for the oval window in

which the stapes footplate has become fixed by disease, a new opening into the internal ear at its most accessible point, that is, over the prominence of the horizontal semicircular canal. It was made possible because of better aseptic technique with the advent of antibiotics to offset the dangers of labyrinthitis, etc.

The new window is brought in contact with the sound-conducting mechanism of the middle ear after parts of the ossicular chain have been removed, by being covered by a flap from the skin adjacent to and continuous with the ear drum. The exact mechanism of transmission of sounds in the new arrangement is not known, but it does result in an improvement of hearing by re-establishment of the phase difference between the two windows in the internal ear. This operation has resulted in an improvement of hearing to what is called a serviceable level (within 30 db. of zero) in about 50% of cases over a five-year period. Because the ossicular chain has been altered, hearing rarely approaches the normal level. It is not known why the relatively small opening in the bony labyrinth wall remains open, but fortunately it does in most cases.

The secondary nerve deafness which is common in many cases of conductive deafness may be arrested by the fenestration operation, but not in every case.

The postoperative care is an important part of the procedure, and the patient must be advised of this in advance because the after-care must be carried out whether or not the operation is a functional success.

STAPES MOBILIZATION

The second operation for non-suppurative ear disease, re-introduced by Rosen in 1953, is called stapes mobilization. It consists of trying to free the footplate of the stapes which has become fixed in the oval window.

The stapedial area is exposed by turning forward a skin flap including the posterior half of the ear drum. This reveals to view the long handle of the incus, the stapes and the oval and round window areas. The accessibility or amount of exposure varies from patient to patient, naturally being the greatest in the patient with a large external ear canal. The operation is carried out under local anæsthesia, which allows for communication between operator and patient during the course of the operation, in order that the operator may judge the effectiveness of his various manipulations.

Success depends upon a number of factors, chief among which is the amount and location of the bridging of the joint between the stapes and the oval window margins. It also depends upon the freedom of the round window niche from disease and upon the intactness of all the other ossicular joints.

One hopes to break through the otosclerotic focus or to fracture the footplate of the stapes, allowing the remainder of the stapes footplate to vibrate with the ossicular chain. The success of the operation can usually be determined at operation by talking to the patient or by carrying out pure tone hearing tests under sterile precautions.

One of the commonest accidents which defeats the operation is fracture of the crura or arms of the stapes. Because this has happened so often, many methods of attacking the footplate of the stapes directly are described in the literature. The value of many of these procedures is not yet established.

The manipulation of the stapes has resulted in improvement in hearing in about 25% of cases, in some reaching the normal level. It is too soon to say how permanent the improvement will be. A word of caution is in order, because imprudent manipulation in the region of the stapes may damage the internal ear structures and result in additional and permanent loss of hearing.

Stapes mobilization is an extremely delicate operative procedure requiring familiarity with the operating microscope. It is relatively easy for the patient, requiring only a few days' hospitalization and very little after-care. If the stapes mobilization operation fails it can, in many cases, be followed in about six months by the fenestration operation.

The matter of operating upon one or both ears is one which is open to question. My own feeling is that this type of surgery is in the early stages of its development and that it will continue to improve. In some cases, the stapes mobilization operation has given better hearing than the fenestration operation. Those patients who have had both ears fenestrated cannot avail themselves of mobilization. The second ear should be held in reserve for yet other advances which we hope are just around the corner.

SELECTION OF CASES

As physicians you are naturally interested in which of your hard-of-hearing patients can avail themselves of these operations. It has been pointed out that an operation for restoration of hearing cannot be successful if the deafness is chiefly of the nerve or perceptive type. The most important single test is to determine the state of the patient's bone conduction. In a middle ear deafness the bone conduction is normal or even better than normal, whereas if there is nerve deafness the bone conduction is less than normal. If your own hearing is normal, a comparative estimate of the patient's bone conduction in an ordinary room can easily be made by using either a 512 or 1024 cycle tuning fork. The stem of the vibrating tuning fork is held alternately on your own and on the patient's mastoid process. If the patient hears the fork by bone conduction for an appreciably longer time than you do, he probably has a middle ear deafness. If you hear the fork longer by bone conduction than does the patient, he probably has a nerve deafness.

This is a rough test which will help you decide whether it is worth your patient's while to make a long or difficult trip to consult an otolaryngologist for a more accurate assessment of his operability.

HEARING AIDS

We have referred to hearing aids only to state that for many types of nerve deafness they are unsatisfactory. It would be unfair not to mention the

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great improvements that have been made in hearing aids, especially in the matter of decreasing size and of increasing the power. This was made possible first by the vacuum tube and later by the introduction of the transistor.

Hearing aids were built into spectacle frames, at first because people would readily acknowledge vision difficulties (even some with normal vision) who were loath to admit to a hearing loss. It has been found, however, that a great advantage of the eyeglasses is that the receiver of the hearing aid is protected from the disturbance of clothes rubbing. Furthermore, it has been found that with decreasing size, two hearing aids can be mounted, one in each frame, and this more nearly simulates normal binaural hearing. The patient recovers his ability to detect sound sources and he may have better discrimination of sound when the binaural hearing aid is worn.

A hearing aid can be worn successfully by any patient whose hearing loss might be lessened by middle ear surgery. An operation which may not restore hearing to the serviceable level may make it possible for a patient to wear a hearing aid more effectively.

Dr. Howard House has suggested a simple homespun method of determining a patient's suitability for a hearing aid. Use an old-fashioned speaking tube in one ear and speak very softly into the tube while making a distracting noise in the other ear. If a patient does get improved hearing under these conditions, the probabilities are that he will be a good candidate for a hearing aid.

These advances in otolaryngology have taken place within the last 20 years, a short time in the world of science. May we not dare hope that, if we establish research laboratories and make available research as a part of the resident training program in otolaryngology, we are on the threshold of still greater progress—both in our knowledge of the causes and in our ability to treat lesions affecting hearing, one of God's most precious gifts.

COLLEGE OF GENERAL PRACTICE OF CANADA

GENERAL PRACTICE RESIDENCIES

THE FOLLOWING HOSPITALS have cooperated with the College of General Practice by establishing General Practice Residencies, which are senior internships whose programs of training are designed to prepare doctors for general practice.

ALBERTA:

Holy Cross Hospital, Calgary, Alta.; Sister C. Gauthier, Superior and Administrator.

Misericordia Hospital, 9830-111th Street, Edmonton; Dr. A. J. Brunet, Medical Director.

St. Michael's General Hospital, 13th St. and 9th Avenue S., Lethbridge; Sister M. Consolata, Administrator.

BRITISH COLUMBIA:

Royal Jubilee Hospital, Victoria; Dr. J. L. Murray Anderson, Medical Administrator.

St. Joseph's Hospital, Victoria; Dr. E. N. Boettcher, Medical Superintendent.

MANITOBA:

St. Boniface Hospital, St. Boniface; Dr. Paul L'Heureux, Medical Director.

Misericordia General Hospital, Winnipeg; Dr. Jack McKenty, Secretary of Executive Staff.

Victoria Hospital, Winnipeg; Mr. G. B. Rosenfeld, Administrator.

NEW BRUNSWICK:

Saint John General Hospital, Saint John; Dr. Carl R. Trask, Director.

NOVA SCOTIA:

Aberdeen Hospital Commission, New Glasgow; Dr. H. C. McKay, Medical Superintendent.

ONTARIO:

Belleville General Hospital, Belleville; Mr. Kenneth E. Box, Administrator.

Hôtel-Dieu Hospital, Cornwall; Sister St. M. Magdalen, Administrator.

Northwestern General Hospital, Keele St., Toronto; Dr. V. C. Malowney.

Hôtel-Dieu of St. Joseph, 1030 Ouellette Ave., Windsor, Ont.; Sister R. M. Prieur, R.N., Assistant Administrator.

Ottawa General Hospital, Bruyère Street, Ottawa; Dr. J. Paul Laplante, Medical Director.

The General Hospital of Port Arthur, Port Arthur; Mr. J. A. McNab, Administrator.

St. Thomas-Elgin General Hospital, St. Thomas; Mr. Bertram G. Thacker, Administrator.

St. Joseph's Hospital, Sarnia; Sister M. St. Paul, Superintendent.

New Mount Sinai Hospital, 550 University Avenue, Toronto; Mr. Sydney Liswood, Administrator.

St. Joseph's Hospital, Toronto; Sister M. Estelle, Superintendent.

Toronto East General and Orthopædic Hospital, Coxwell at Sammon Avenues, Toronto 6; Mr. E. R. Willcocks, Superintendent.

QUEBEC:

Montreal General Hospital, Montreal; Dr. William Storrar, Medical Director.

Notre-Dame Hospital, Montreal 24; Dr. J.-R. Boutin, Medical Director.

Royal Victoria Hospital, Montreal 2; Dr. Ronald V. Christie, Physician-in-Chief.

L'Hôtel-Dieu de Québec, Quebec; Dr. J.-B. Jobin, Medical Director.

Hôpital St-Joseph, 779 Ste-Julie, Trois-Rivières; Dr. J. J. Laurier, Medical Director.

SASKATCHEWAN:

St. Paul's Hospital, Saskatoon; Sister A. Lachance, Administrator.

Regina General Hospital, Regina; Dr. H. E. Appleyard, Superintendent.

Association Notes

P.R. AID FOR DOCTORS' OFFICES

PROBABLY the greatest threat to good medical public relations is misunderstanding. The patient who receives medical treatment without understanding what it is or why he receives it, or the one who receives an unexpectedly large perhaps undetailed bill, is a potential source of complaints about the profession.

The solution is prevention of misunderstanding by enlightenment. Let the doctor explain his treatment and why he prescribes a certain course of action.

More important, let him discuss his fees with the patient, preferably in advance. By attempting to estimate his own bill and, if possible, anticipating hospital and drug costs, the doctor can eliminate many damaging complaints.

Unfortunately, too often the doctor is loath to introduce discussion of fees.

Realizing this—and aware that mutual understanding between doctor and patient is essential to good medical service and good public relations—the Canadian Medical Association's Committee on Public Relations has produced a plaque for use in the doctor's office inviting patients "to discuss frankly . . . any questions regarding service or fees". The wording is as follows:

> **I invite you to discuss frankly with me any questions regarding my service or fees.**
>
> *The best medical service is based on a friendly mutual understanding between doctor and patient.*

The plaque measures 9" by 6¾". The wording in gold is printed on walnut-finish paper fused to heavy ⅛" board. Edges of the plaque are bevelled and gilded. An easel mounted on the back permits standing the plaque on the desk, or hanging it on the wall.

The plaques are now ready for distribution and one free copy in English *or* French will be sent on request.

Request for plaques should be sent to the Secretary of the C.M.A. Division in your area—or to Mr. K. C. Cross, Assistant Secretary, The Canadian Medical Association, 150 St. George Street, Toronto 5, Ontario.

POUR LE MEDECIN

L'incompréhension est probablement l'obstacle le plus fréquent qui puisse fausser les relations entre le médecin et ses clients. Le patient qui ignore la raison des traitements qu'il reçoit ou celui à qui on présente une note élevée et non détaillée peut se plaindre de la profession médicale.

La solution de ce problème est fondée sur la prévention. Que le docteur explique la raison de tel ou tel traitement, ou justifie ses ordonnances, et le froid se dissipera.

Il doit être prêt à discuter ses honoraires avec le patient, préférablement à l'avance. De plus, en tentant d'estimer sa note, et si possible d'évaluer par anticipation les frais d'hôpital et des produits pharmaceutiques, le médecin peut éliminer beaucoup de critique de la part des patients. Il est regrettable que trop souvent le médecin se refuse de parler de ses honoraires et de les expliquer à son malade.

Fort de cet état de chose et sachant qu'une bonne entente entre le médecin et son client est essentielle à des soins médicaux convenables, le comité des relations extérieures de l'Association médicale canadienne offre à ses membres une plaque assurant les patients qu'ils ont l'entière liberté de lui parler de toutes questions relatives à ses soins ou à ses honoraires. La plaque si lit comme suit:

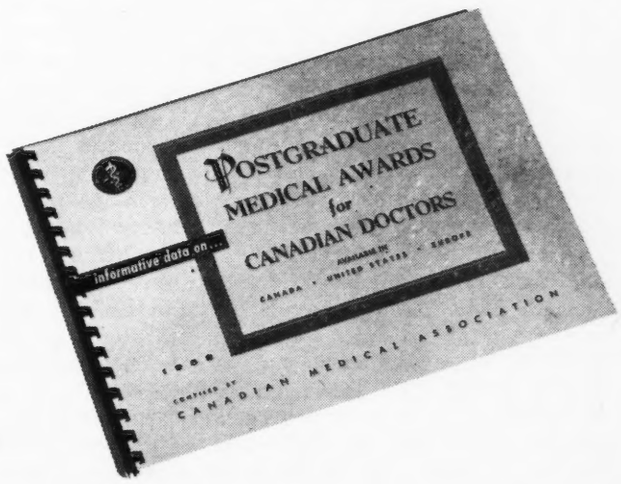
> **Vous avez l'entière liberté de me parler de toutes questions relatives à mes soins ou à mes honoraires.**
>
> *Les meilleurs soins médicaux sont le fruit de la bonne entente entre le médecin et son client.*

Cette plaque mesure 9" × 6¾"; le lettrage doré est imprimé sur du papier à l'imitation de chêne et apposé à une planchette de ⅛ de pouce. Les bords de la plaque sont biseautés et dorés. Un support monté à l'arrière permet de poser cette plaque sur un bureau ou de la suspendre au mur. Ces plaques vous sont offertes gratuitement et vous pouvez recevoir un exemplaire en anglais ou en français sur demande.

Veuillez vous adresser au secrétaire de l'A.M.C. dans votre division ou écrire à monsieur K. C. Cross, secrétaire adjoint, Association Médicale Canadienne, 150 St. George St., Toronto 5, Ontario.

POSTGRADUATE MEDICAL AWARDS FOR CANADIAN DOCTORS

Arranged alphabetically by field of postgraduate study, the pages of this reference manual list the nature of the award, its amount, the conditions which apply, and the source of further detailed information.



A limited number of these manuals are still available for members of the Association who are planning their postgraduate training. Requests for individual copies should be sent to the General Secretary, 150 St. George Street, Toronto, Ontario.

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SCIENTIFIC EXHIBITS AT EDINBURGH

The British Medical Association announces that a Scientific Exhibition has been arranged as a feature of the Joint Annual Meeting of the B.M.A.-C.M.A. in Edinburgh, July 18-24, 1959.

Members of the Canadian Medical Association who have material suitable for display are invited to contribute to the Scientific Exhibition. Preliminary application for exhibit space should be made to the Secretary of the British Medical Association, B.M.A. House, Tavistock Square, London, W.C. 1, from whom a detailed application form with full information may be obtained. Entries close *December 31, 1958.*

MEDICAL MEETINGS

LE XXVIIIe CONGRES DE L'ASSOCIATION DES MEDECINS DE LANGUE FRANCAISE DU CANADA

The following report has been offered to us through the courtesy of "l'Union Médicale".

C'est dans le site enchanteur de Saint-André-sur-Mer, au Nouveau-Brunswick, qu'avait lieu cette année en septembre le XXVIIIe Congrès de l'Association des médecins de langue française du Canada. Rendez-vous acadien réussi en tous points: très nombreux participants représentant toute la gamme des déplacements de l'Alberta jusqu'au Maine, épouses ravies d'être environnées de fleurs, d'une végétation exubérante face à la mer que le moindre rayon de soleil venait animer, programme scientifique et social se déroulant sereinement et avec efficacité. Bref un congrès conçu et réalisé dans un climat d'amitié.

Parmi les invités officiels, on remarquait à la séance d'ouverture outre l'Honorable Hugh John Flemming, premier Ministre du Nouveau-Brunswick et Son Exc. Monseigneur Norbert Robichaud, archevêque de Moncton, l'ambassadeur de France au Canada, M. Francis Lacoste dont la fidélité à nos Congrès est devenue une tradition, ainsi que deux ministres du cabinet provincial de Fredericton. Tous admirèrent l'aisance avec laquelle le président du Congrès, le Dr Georges-L. Dumont maniait les deux langues en cette circonstance et l'autorité souriante et spontanée qu'il sut montrer pendant toute la durée de nos assises.

Nous avons déjà mentionné ici le renom qui précédait la venue du Professeur André Lemaire, délégué officiel du Gouvernement français. Par son assiduité à nos séances scientifiques, l'intérêt de sa communication personnelle sur "la rate dans l'hypertension portale," la bonne grâce avec laquelle il a multiplié ses contacts et ses entretiens avec les congressistes, il a rempli excellement sa mission parmi nous. Je ne saurais entrer dans le détail du programme scientifique et citer les travaux de chacun. Qu'il me suffise de dire que ce programme a illustré, une fois de plus, la valeur du travail d'équipe. C'est le cas, par exemple, d'une communication sur le "Lupus érythémateux aigu" par les docteurs Richard Lessard et Marcel Guay de Québec, et des colloques sur les stéroïdes et sur l'ulcère peptique qui, mobilisant des compétences, ont permis échanges de vues fructueux.

"L'Acadie vous attend" avait écrit le docteur Georges-L. Dumont en nous invitant à ce congrès. Ce n'était pas là une phrase conventionnelle et une très intéressante soirée de films documentaires devait permettre à ceux qui y assistèrent de faire connaissance avec les multiples visages de l'Acadie: ses villes, ses établissements religieux et universitaires, son folklore et ses industries, sa terre rouge et fertile, la vie dangereuse et âpre de ses pêcheurs et tout un peuple parlant et chantant avec la fidélité gravée dans son coeur. Il y a une expression que l'on galvaude un peu facilement: c'est celle "d'assises fraternelles". S'il y a une circonstance où ces mots sont devenus réalité, c'est au cours de cette même soirée de cinéma quand, durant l'entracte un ancien de l'Université Saint-Joseph entonna des chansons acadiennes—dont "Evangéline"—que toute l'assemblée reprit en chœur. Ajoutons que le cinéma ne se contenta pas d'être "récréatif" au XXVIIIe congrès, et que de nombreux films scientifiques furent régulièrement présentés.

Enfin le dîner de clôture nous permit d'entrevoir de brillantes perspectives d'avenir, tant dans le cadre des relations médicales franco-canadiennes destinées à connaître une extension nouvelle, que par le dynamisme de notre Association qui entend être un exemple de la bonne santé qu'elle défend et prêche autour d'elle. Le congrès de Saint-André-sur-Mer a marqué une autre phase importante dans nos relations professionnelles à travers tout le Canada. Il a montré à quel point l'Association des médecins de langue française était un lien vivant d'un océan à l'autre et que derrière un nom symbolique il y avait une réalité objective, solidement encadrée et qui ne demande qu'à grandir, à multiplier ses initiatives et à soutenir notre prestige culturel pour le plus grand bien de tous.

DR PIERRE SMITH,
President, A.M.L.F.

THE SIXTH INTERNATIONAL CONGRESSES ON TROPICAL MEDICINE AND MALARIA

The Sixth International Congresses on Tropical Medicine and Malaria took place in Lisbon from September 4-13, 1958 under the high patronage of His Excellency the President of the Portuguese Republic, Admiral Americo Deus Rodrigues Thomaz. The Honorary Committee included all the members of the cabinet and other dignitaries of the government, the university, scientific societies and the city.

The president of the Congresses was Dr. Joao Praga de Azevedo (Portugal), and the general secretary, Dr. Manuel Reimao da Cunha Pinto.

Members from 56 countries participated and many known figures in the field were present, such as Sir Aldo Castellani, Sir Philip Manson-Bahr, R. M. Chaudhari, B. G. Maegraith, Henri Galliard, A. Salazar Leite, J. Orskov, T. M. Rivers, E. T. C. Spooner, J. Travassos, Marcel Vaucel, Elsdon Dew, Kojo Okabe, Fred L. Soper and many others. Members from Canada were T. W. M. Cameron and Eugene Meerovitch, Montreal, and Michael Lenczner and Roy C. Anderson, Toronto.

A colourful opening ceremony took place on September 5 at the National Assembly (Palacio de S. Benito) under the presidency of His Excellency the President of the Republic. Addresses were read by His Excellency the Overseas Minister of Portugal, Prof. B. G. Maegraith, and Prof. Fraga de Azevedo.

The scientific sessions went on in four sections and all subjects relating to tropical and parasitological medicine were discussed, with reference to soil, seed, vectors, pathology, and improved methods of diagnosis and treatment. Problems such as anæmias and abnormal hæmoglobins, gastro-intestinal infections, mycobacterial infections, schistosomiasis, and malaria were widely reviewed. The need for eradication of the causative factors rather than treatment was emphasized; modern disinfectants, improved living conditions since World War II, and widespread teaching of hygiene appeared to be the answer to many problems. Progress in communications on the other hand had widened the field of these diseases.

Canadian contributions included papers on:

1. Hydatid cyst disease by Prof. T. W. M. Cameron of McGill University, Montreal. This subject was treated most completely with an impressive and vast documentary material and series of slides. The meeting expressed their keen appreciation and admiration of Prof. Cameron, an authority on the subject.

2. The impact of tropical and parasitic diseases on the medical centre, Toronto, by Dr. Michael Lenczner of the Toronto General Hospital, University of Toronto. It demonstrated the spread of these diseases to temperate climates, especially in countries with a great number of immigrants which represent the receiving line. Special emphasis was laid on cysticercosis with documentary material—radiographs and slides—a subject studied in this centre by Drs. Trevor Owen, D. G. Wollin and M. Lenczner. This theme created great interest and was discussed again in a separate meeting.

On Sunday, September 7, the members of Congress were invited to the University of Coimbra, the third oldest in the world (first came Bologna, Italy and second Salamanca, Spain) and in a very impressive ceremony the Laveran prize for work on malaria was presented to Dr. Emilio Pampana (Italy), staff member of WHO, for his excellent work in eradication of malaria.

The social side of the Congresses and the ladies' programs were arranged with grace and most lavishly by the Portuguese members of the Congresses and their ladies, the government and the city dignitaries.

PUBLIC HEALTH

EPIDEMIC OR UNUSUAL COMMUNICABLE DISEASES IN CANADA

During the week ending August 30, 1958, the Epidemiology Division of the Department of National Health and Welfare, Ottawa, received the following surveillance reports of epidemic or unusual communicable diseases.

Poliomyelitis

MANITOBA—Dr. R. M. Creighton, Director of Preventive Medical Services, has forwarded further information on the paralytic poliomyelitis situation in Manitoba this year. To August 23, 33 cases had occurred, 27 of which were in Winnipeg. This represents 47% of the total cases reported in Canada this year. Of the 23 cases that occurred up to August 16, two patients had received three doses of vaccine. The other 21 paralyzed patients, five of whom are in respirators, had never received any vaccine. The great majority of cases so far are in the pre-school and adult age groups.

Rabies

WINNIPEG—Dr. Roper Cadham, Medical Officer of Health, has reported one case of rabies in a gopher. A child bitten by this gopher is receiving vaccine. Four other children were bitten by gophers, but the animals could not be traced. It is intended to give vaccine to those children also.

Dr. W. A. Moynihan, Health of Animals Division, Department of Agriculture, Ottawa, states that this is the first time that rabies has been diagnosed in a gopher. He also stated that gophers that have bitten children should be suspected of rabies, as they usually do not bite.

Infectious Hepatitis

ALBERTA—Approximately 120 cases of infectious hepatitis have occurred in the last two months in the Lethbridge area.

Indian and Northern Health Services

Dr. P. E. Moore, Director, Indian and Northern Health Services, and Dr. N. Gillison of Northern Health Services, have forwarded the following reports:

Clearwater Lake, Man.—Twenty cases are reported of infectious hepatitis of which 13 were in Eskimos, five in Treaty Indians and two in non-Treaty Indians.

Stoney Creek Reserve—Sixteen cases of infectious hepatitis have occurred on the Reserve.

Measles

Cambridge Bay, N.W.T.—Several outbreaks of measles during the summer are reported. At Cambridge Bay 154 cases have occurred of which 22 cases were complicated by bronchopneumonia. Other outbreaks occurred at DEW Site 16 (100 miles from Cambridge Bay), 8 cases with 2 cases of bronchopneumonia; Richardson Island, 18 cases (90% of the population) and 7 cases of bronchopneumonia; Lady Franklin Point, Victoria Island, 7 cases and 4 cases of bronchonpneumonia.

LETTER TO THE EDITOR

MINIATURE CHEST FILMS FROM MIRROR AND LENS CAMERAS

To the Editor:

In a paper entitled "Gonadal Dose from Miniature Chest X-Rays", published in the April 15, 1958, issue of the *Canadian Medical Association Journal*, Johns and Wilson reported on their findings in respect to exposures required to produce 70-mm. chest films of comparable densities, using a mirror camera and a lens camera. It was found that the newer mirror camera required between one-quarter and one-fifth of the exposure required to produce films of the same density using the lens camera, all other factors being constant.

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Density of films only was dealt with in the report and it was suggested to me by Dr. Johns that a further brief report be submitted for publication in regard to the radiographic quality of the films.

Twenty successive patients were later x-rayed, using both cameras for each patient and employing the same equipment as described in the earlier report. The film used in the two cameras was again of the same emulsion number, and the two strips of film were processed simultaneously. Each patient was x-rayed first on the mirror camera unit, the duration of the phototimed exposure being determined by a cycle counter, and then x-rayed on the mirror camera using an exposure four times as long. The resulting miniature films of each patient were checked on a densitometer by Dr. Johns and found to be comparable. The films were then compared at the Gage Institute Chest Clinic and it was considered that radiographically they were of good quality, and equally satisfactory for detecting abnormality.

It was therefore concluded that, other factors being equal, the mirror camera permits good 70-mm. chest films to be made with one-quarter of the x-ray exposure to the patient required for similar films made with the lens camera.

H. T. McCLINTOCK, M.D.

Gage Institute Chest Clinic,
Toronto, Ont.,
August 28, 1958.

OBITUARIES

DR. ALFRED TURNER BAZIN

AN APPRECIATION

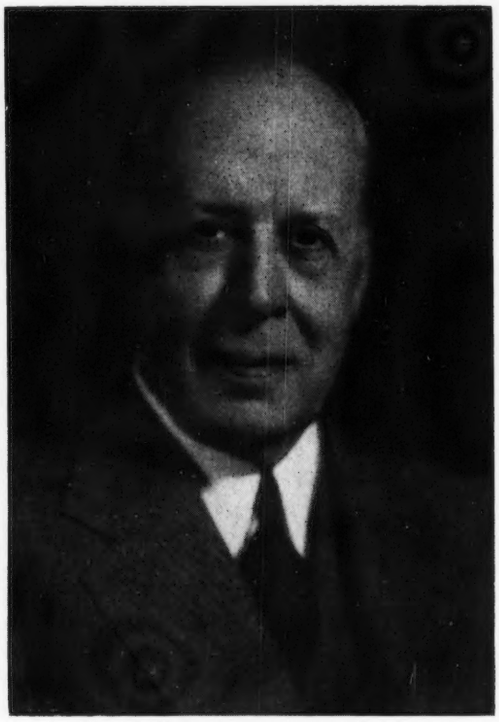
At a meeting of the Council of the Canadian Medical Protective Association, the following appreciation of Dr. A. T. Bazin was read out:

It is our sad duty at this meeting of Council to give official expression as a Council to the grief and sense of loss we have all experienced in the death of our Honorary Life President, Dr. Alfred T. Bazin.

Many tributes will be paid Dr. Bazin and will contain the details of a singularly useful life: they will tell of the recognition that was earned by a life devoted primarily to medicine and of a career that, in retrospect, may well prove to have been one of the most important in the history of Canadian medicine; undoubtedly too they will mention his wide interests outside medicine. So tonight we can think only of Dr. Bazin's contribution to the welfare of the medical profession through this Association.

Some members of this Council had the privilege of close contact and friendship with Dr. Bazin and have been much influenced by him, some knew him less intimately, but all members of Council have recognized his influence and been grateful for it. All of us will think at once of the number of occasions on which it was wondered what Dr. Bazin would think of important matters under discussion, and when decisions were reached we will remember the number of times they were submitted to Dr. Bazin for comment before they were considered final. The pervasiveness of his influence and how great it was will be more apparent if it is remembered that it was exercised from a distance; in recent years Dr. Bazin never attended a meeting of Council, and his opinions had to reach us by letter or, much less often, during short, casual personal contacts.

Dr. Bazin's influence was so great and so steady because of the man himself. His qualities of mind need no comment; the heights he reached in his profession are sufficient evidence. His qualities of heart shone through his actions, for all who worked with him and were important in his work with this Association. He



Dr. Alfred Turner Bazin

was a man of complete personal honesty, who assumed the same quality in others and whose example almost forced the same standard on his fellowmen. He was kindly in his thoughts about others and in those actions that affected them. His kindliness was natural, part of the man himself, qualified and modified by his other exceptional attributes; we saw it applied to the manner and degree of help that he thought the Association should give its members. Repeatedly over the years the Association heard from Dr. Bazin that he thought help ought to be extended, where perhaps otherwise it might have been withheld or given only in part; he constantly emphasized the doctrine that the Association existed to help in its own field and that if it failed to do so it failed not only a member but itself and the profession of which it was a part. Yet he was no sentimentalist; his shrewdness and practicality saved him from championing poor causes; he was adamant in his refusal to allow the Association to be imposed on. And he would not have the Association a part of anything detrimental to the moral or ethical standards of the profession.

His wide experience contributed to the development of the Association, to revisions of its By-laws, to the formulation of policy—and to the no less important occasions when circumstances should be allowed to modify policy. He liked clarity of thought and statement and, indeed, insisted on them in the things that were written for his perusal; he did not hesitate to make a good-humoured request that writing be clarified.

Dr. Bazin's active guidance in Association affairs will be missed. Such a person is irreplaceable, but his example and the principles on which he insisted will remain a part of the Association.

As well as expressing its own sense of loss, Council and the Association wish to extend to Mrs. Bazin and the members of Dr. Bazin's family its sincere sympathy in their bereavement.

DR. OTTO M. DROUILLARD, 56, died on August 20. He graduated in medicine from the University of Western Ontario in 1928, and practised in Belle River. He did postgraduate work in Illinois State Hospital, specializing in ear, nose and throat work. He had been a specialist in Chatham since 1937.

Dr. Drouillard is survived by his widow and two stepchildren.

DR. GASTON LAPIERRE, 73, died on August 30. He was born in St. Hyacinthe, Quebec, and completed his early studies there. He received his medical degree from the University of Montreal in 1908. After practising in St. Hyacinthe for several years, he moved to Montreal in 1918 and became affiliated with St. Justine's Hospital. In 1921, Dr. Lapierre went to France and completed postgraduate courses in pædiatrics. On returning to Montreal, he became chief of pædiatrics at St. Justine's, a post he held from 1928 to 1957. He returned to Paris for further studies in 1931 and later became professor of pædiatrics at the University of Montreal; he was attached to the University from 1937 until 1950.

Dr. Lapierre is survived by his widow and one son.

DR. JAMES A. MUIR, 53, died on August 27, in Victoria General Hospital, Halifax, after a brief illness. He was a graduate of the Dalhousie Medical School, and had practised medicine in Truro since his return from service overseas in the Royal Canadian Army Medical Corps during World War II. He was recently appointed vice-president of the Nova Scotia Heart Association.

Dr. Muir is survived by his widow, three sons and two daughters.

DR. EMERSON TROW

ELOGE FUNEBRE

A Toronto, dans la soixante-douzième année de son âge, est décédé le Dr Emerson Trow.

Le Dr Trow était un dermatologiste averti et compétent qui fut de nombreuses années professeur de dermatologie à la faculté de médecine de Toronto.

Le Dr Trow était dans le véritable sens du terme un "gentleman", toujours souriant et répondant avec bonté et complaisance à toutes les questions posées. Son sourire engageant n'était que la transcription extérieure d'une philosophie qui se refuse à être triste.

Le Dr Trow se faisait un devoir d'assister à tous les congrès de l'Association dermatologique canadienne. A deux reprises il avait assisté à deux de ces congrès tenus à Québec. Sa présence était un encouragement aux dermatologistes québecois qui n'oublieront pas de sitôt cet homme bâti en athlète, souriant, et prototype du parfait gentilhomme.

A sa veuve et à ses enfants, particulièrement à son fils, dermatologiste lui aussi, les dermatologistes de Québec offrent leurs plus sincères condoléances et les prient de croire que le souvenir du Dr Trow vivra longtemps dans leur mémoire. EMILE GAUMOND

DR. JAMES H. WOOD, 79, died on September 1. He was educated at the University of Western Ontario and graduated in medicine from the University of Toronto in 1908. He practised in Toronto, was staff surgeon at the Western Hospital, and lectured on surgery at the University of Toronto until his retirement after World War II. During World War I he was commanding officer of No. 2 Field Ambulance with the Canadian Army Medical Corps overseas.

Dr. Wood is survived by his widow, two sons and three daughters.

DR. CHEVALIER JACKSON, the celebrated bronchoscopist, died on August 16 in Temple University Hospital, Philadelphia, aged 92. Practically his whole medical career was connected with laryngology, for he became professor of laryngology in the University of Pittsburgh in 1912, and was then subsequently professor of laryngology in Jefferson Medical College from 1916 to 1930 and professor of clinical bronchoscopy at Temple University School of Medicine, Philadelphia. He will go down to history as the man who made bronchoscopy and œsophagoscopy practicable and safe.

PROVINCIAL NEWS

BRITISH COLUMBIA

The new Queen Alexandra Solarium at Gordon Head in Victoria, built at a cost of $900,000, has been officially opened. It replaces the Mill Bay solarium which has done wonderful work for crippled children for over thirty years. The new solarium will have ultimately a 96-bed capacity, 80 at present, instead of the 30 at Mill Bay.

The Tranquille Sanitarium, which housed tuberculosis patients for 50 years, and has recently ceased acting in this capacity, is to become a school for mental defectives. The Hon. Eric Martin, Minister of Health and Welfare of B.C., made this announcement.

The necessity for Tranquille, which has really led the fight against tuberculosis in B.C., and has achieved far more success in its work than the average B.C. citizen knows, is not now so great, because Pearson Memorial and other hospitals, with the great improvements in treatment, can handle the situation adequately.

Mr. Martin is, we feel, much to be congratulated on this foresighted and intelligent decision.

When a public gets the facts, and is roused to action, it can do a great deal. North and West Vancouver for some years have suffered greatly for lack of hospital accommodation, and have been clamouring in a general way for it. A North and West Vancouver Hos-

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pital Society came into being, and under its president, Mr. Robert R. Keay, went all out to educate the public as to the facts, hold plebiscites and so on. The authorities cannot be said, or so we understand, to have encouraged the idea as it meant the ultimate expenditure of some $6,000,000 – but finally put the by-law to the vote. A 90% vote in favour was the result. There were three districts involved and the vote was overwhelming in each.

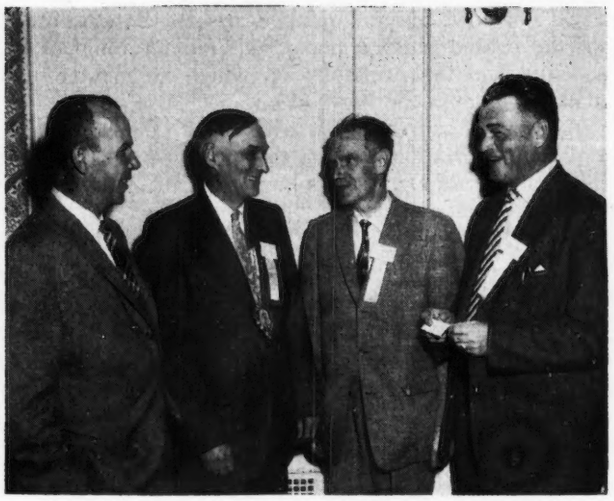
The children of B.C., by donations of a dime per head, have collected $18,000 to help ill and disabled children at the Queen Alexandra Solarium in Victoria and the Princess Margaret Children's Village (the former Preventorium) in Vancouver. Libraries will be built, visual equipment will be provided, and there will be toys for the children.

NEW BRUNSWICK

At the 78th Annual Meeting of the N.B. Medical Society held at the Algonquin Hotel, St. Andrews, the following officers and committees were elected: President, Dr. R. B. MacKenzie, Nekcastle; First Vice-president, Dr. Paul Melanson, Moncton; Second Vice-president, Dr. S. R. Webber, Calais, Maine; Treasurer, Dr. Norman Skinner, Saint John; Secretary, Dr. F. L. Whitehead, East Riverside; Executive Committee: Drs. B. Pothier, Dalhousie; E. Stiles, St. Stephen; B. L. Jewett, Fredericton; J. A. Wilson, Woodstock; Ian MacLennan, Moncton; F. H. George, Saint John; W. B. Orser, Bathurst; Claude Gaudreau, Edmundston; T. S. Dougan, Sussex; J. C. Duffy, Chatham; N.B. Representative on C.M.A. Council, Dr. G. M. White; The Medical Council of New Brunswick: Drs. Georges Dumont, Campbellton; H. S. Wright, Fredericton; J. R. Nugent, Saint John; V. A. Snow, Hampton; R. M. Pendrigh, Saint John; Ian MacLennan, Moncton; A. Robichaud, Tracadie; Emery Legère, Moncton; and E. F. Woolverton, Woodstock. The Hon. J. F. McInerney, M.D., Minister of Health for N.B., represents the Provincial Government as the tenth member of this Council.

The Harvey Studio, St. Stephen, N.B.

Left to right: Dr. R. B. MacKenzie, Newcastle, President-Elect, 1957-58; Dr. F. C. Jennings, Saint John, President, 1957-58; and Dr. Ross Wright, Fredericton.



The Harvey Studio, St. Stephen, N.B.

Left to right: Dr. R. B. MacKenzie; Dr. Arthur VanWart, President, C.M.A., 1958-59; Dr. F. C. Jennings; and Dr. F. L. Whitehead, Secretary, N.B. Medical Society.

The scientific program included papers by Dr. Stuart Gordon on burns and on traumatic lesions of the hand, and papers by Dr. William A. Oille on the role of anticoagulant therapy in practice today. A panel discussion on non-obstructive jaundice was led by Dr. A. L. Donovan, with participation by Drs. W. A. Oille, Kenneth C. Rodger, Garfield Moffatt and Ian A. MacLennan.

Speakers on a symposium on prepaid medical care were: Mr. C. Howard Shillington and Drs. Norman S. Skinner, S. D. Clark and J. A. MacDougall.

The C.M.A. was ably represented by the President, Dr. A. F. VanWart, the Assistant General Secretary, Dr. A. F. W. Peart, and Mr. K. W. Cross, Public Relations Secretary. It was regretted by his many friends in New Brunswick that the General Secretary was unable to be with us at our Annual Meeting.

Miss Ruth Cook Wilson of Moncton was elected an honorary member of the N.B. Medical Society at the Annual Meeting. Miss Wilson was one of the founders of Maritime Hospital Service Association and its first executive director. Her election to honorary membership recognizes her contribution to the development of prepaid medical care. She was a former administrator of the Moncton Hospital and chairman of the Canadian Council of Blue Cross Plans. She is also a member of the American College of Hospital Administrators, and was chairman of the N.B. Health Survey Commission. Miss Wilson was awarded the honorary degree of doctor of laws by St. Francis Xavier University in Antigonish, Nova Scotia.

Dr. Georges Dumont of Campbellton, President of L'Association des Médecins de Langue Française du Canada, welcomed many distinguished guests from many provinces of Canada and from the United States to the 28th convention of the Association held at the Algonquin Hotel, St. Andrews, in early September. Physicians and surgeons from New Brunswick presented papers, took part in round table discussions and chaired the various sessions. His Excellency, M. Francis Lacoste,

the French Ambassador to Canada, was in attendance. The election of officers resulted in the following slate: Director, Dr. Emile Blain, Montreal; Secretary-General, Dr. Hermile Trudel, Montreal; President, Dr. Pierre Smith, Montreal; First Vice-president, Dr. Ernest Beuglet, Windsor, Ont.; Second Vice-president, Dr. Pierre Jobin, Quebec; Third Vice-president, Dr. J. Euclide Léger, Montreal; Fourth Vice-president, Dr. Gérard J. Breton, North Battleford, Sask.; Secretary, Dr. Origène Dufresne, Montreal; Treasurer, Dr. André Leduc, Montreal.

Dr. Emery Legère of Moncton has been elected President of the N.B. Chapter of the College of General Practice of Canada. Other officers are: Dr. Percy Losier, Chatham, Vice-president; Dr. D. A. C. Malcolm, Secretary; and Dr. Everett Reid, Plaster Rock, Treasurer.

Dr. Lynn E. Bashow has been appointed Director of Forest Hill Rehabilitation Centre in Fredericton.

The New Brunswick Division of the Defence Medical Association of Canada held their Annual Meeting at St. Andrews. The officers for 1958-59 are: President, Major A. G. Chaisson, Fredericton; Vice-president, Lt.-Col. F. H. George, Saint John; Secretary, Lt.-Col. R. J. Brown, Moncton. Major G. E. Maddison of Saint John was appointed as delegate from N.B. to the Annual Meeting of the Defence Medical Association at Ottawa.

Dr. J. M. Barry of Saint John retired from his position as registrar of the Medical Council of New Brunswick at the Annual Meeting of the N.B. Medical Society at St. Andrews. He has held this position for the past 23 years. That is a long period of service in such a responsible post, but it is a bit unusual when it is known that this gentleman is in his 91st year—and as a good Maritimer, is still going strong. When he presented his final yearly report and his desire to retire, he received a standing ovation from the Society, and later in the meeting a presentation of a clock and the best wishes of all members of the Medical Society and representatives from the C.M.A. and the Maine Medical Society.

The Hospital Services Commission which will administer the Hospital Care Insurance Act in New Brunswick is headed by the Hon. J. F. McInerney, M.D., Minister of Health; Dr. J. A. Melanson, Chief Medical Officer; and Dr. F. C. Jennings, Saint John. The three other members are Mr. Leonard Lockhart, Moncton, Mr. J. L. Black, Sackville, and Mr. J. R. Shiels, Saint John.

A. S. KIRKLAND

SASKATCHEWAN

Dr. D. G. McKerracher, Professor and Head of the Department of Psychiatry, College of Medicine, University of Saskatchewan, has been appointed to the Advisory Panel on Mental Health of the World Health Organization. He will serve for five years.

BOOK REVIEWS

VARIED OPERATIONS. Herbert A. Bruce, Toronto. 366 pp. Illust. Longmans, Green & Co., Toronto, 1958. $6.00.

It is not often in recent years that this reviewer has burned the midnight oil to finish a book, but this autobiography of Dr. Herbert Bruce proved so absorbing that domestic admonishments were completely disregarded. Herbert Bruce, who celebrated his 90th birthday on September 28, 1958, has lived a full life which encompasses the emergence of Canada as a nation and which in his professional career extends from the introduction of antiseptic surgery to the availability of the latest antibiotics. He has made outstanding contributions both to the public life of Canada and to the medical profession. An individualist rather than a team player, he was often the centre of a stormy controversy and it is fascinating to read his own account of his activities as Special Inspector General of Canadian hospitals and medical establishments in World War I, his difficulties with the newly appointed Professor of Surgery at the University of Toronto, his establishment of the Wellesley Hospital and his accurate recollection of the many other medical issues in which he was a vocal protagonist. We are taken behind the scenes in the Banting-Best-MacLeod controversy which marked the introduction of insulin and we have a revealing glimpse of Dr. Bruce's part in frustrating the demands of drugless practitioners for unwarranted privileges in Ontario.

In accepting the appointment of Lieutenant-Governor of Ontario in 1932, the Honourable Dr. Bruce entered upon what he has termed a new occupation. He fulfilled the duties of the office with great distinction until 1937, but again he was involved in a dispute with Mitchell Hepburn, the flamboyant Premier of Ontario who was determined to close Government House in the interests of economy.

With the outbreak of World War II, Herbert Bruce, an ardent imperialist, felt strongly that Canada's war effort was likely to be impaired by the half-hearted efforts of the Federal Government under Mackenzie King. The dissolution of Parliament in January 1940 gave him the opportunity to express his political convictions and he was elected Conservative Member of Parliament for the riding of Parkdale. Commencing his career as a parliamentarian at the age of 72, Dr. Bruce served as a member of His Majesty's loyal opposition throughout the war and resigned his seat after successfully contesting the general election of 1945. Among the freshmen members of the parliament elected in 1940 was another, John Diefenbaker, who has attained considerable distinction, and the foreword to *Varied Operations* is an outstanding contribution from the pen of the current Prime Minister of Canada.

There are many other facts and impressions which could be recorded about this revealing autobiography, but to do so would be to spoil the pleasure of the wide circle of medical readers which the book will attract. Suffice it to say that this is recommended reading for every doctor who is interested in the story of Canadian medicine and surgery as well as in the development of the nation over the past 90 years. The Canadian Medical Association can take great pride in the life and the literature of its most distinguished Senior Member.

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THE IMPACT OF ANTIBIOTICS ON MEDICINE AND SOCIETY. Monograph 2: Institute of Social and Historical Medicine, New York Academy of Medicine. Edited by Iago Galdston. 222 pp. International Universities Press, Inc., New York, 1958. $5.00.

This is a group of essays dealing with antibiotics from a variety of viewpoints—ranging from that of the medical historian to the microbiologist, engineering chemist, epidemiologist, clinician and veterinarian. In all, it indicates very well the impact of antibiotics on our society as a whole, as well as the purely medical and pharmaceutical aspects. It is surprising to learn how long ago various adumbrations of the antibiotic era had been noted. Its rapid recent evolution required the attainment of a certain level in scientific thought and technology. The effect which has been exerted on medical and lay thought is touched upon, and certain correctives are suggested. The annual production of antibiotics has reached the staggering total of 800 tons, a surprising amount of which is used in animal husbandry and veterinary medicine. A whole new industry has appeared out of nowhere, with a capital value now reckoned in the billions and an annual product worth more than 200 millions at the manufacturing level. The benefit accruing to mankind is not so easy to quantitate, but this volume offers food for thought on this point.

POLYMYOSITIS. John N. Walton, King's College, University of Durham, England, and Raymond D. Adams, Harvard University, Boston, Mass. 270 pp. Illust. E. & S. Livingstone Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1958. $5.50.

This volume deals with a group of conditions, none common, which have recently been the object of much attention. The authors have taken the opportunity to give an extended and modified account of the picture of polymyositis presented in a previous book of which Dr. Adams was co-author.

The conditions discussed include dermatomyositis, polymyositis, paroxysmal and spontaneous myohæmoglobinuria, interstitial polymyositis with "collagen" diseases, calcinosis universalis, menopausal muscular dystrophy and carcinomatous myopathy. The book is based upon a series of 40 cases seen by one or both of the authors, and the histories and pathological findings in these cases are presented in an appendix which occupies almost one-quarter of the book.

The field is reviewed and an attempt made to classify these disorders. The classification, as the authors state, divides the cases arbitrarily into four clinical groups. A detailed analysis of the clinical and pathological features of their own cases is given, and particular mention should be made of the accounts of the electromyographic and pathological findings. The nature of the pathological processes and the relation between these various conditions are discussed. The authors conclude that the majority of the cases fall into one large etiological group closely related to the "collagen" diseases.

The authors assume among their readers a considerable knowledge of the fields upon which they touch and, without presenting much that is new, they discuss the problems of polymyositis in great detail. This makes the book difficult reading but it is a valuable guide to present knowledge of these diseases and to the relevant literature. It is of convenient size, well produced and well illustrated.

NEOMYCIN: Its Nature and Practical Application. Edited by S. A. Waksman. 412 pp. Illust. The Williams & Wilkins Company, Baltimore; Burns & MacEachern, Toronto, 1958. $5.00.

This is the story of neomycin, as told by 35 contributors. It begins with Waksman's account of how he discovered the organism which produces it in 1915, and then goes forward to the identification of the antibiotic itself in 1949. At first it appeared full of promise, being bactericidal and more dependable than streptomycin, but then it proved to be endowed with toxic properties affecting the ear and kidney which were prohibitive as far as its use in tuberculosis was concerned, and which for a time precluded its systemic use in any except the most desperate infections. However, since that time, various things have worked in its favour. Its bactericidal action, coupled with a rather broad spectrum, a very low sensitization potential, and stability in solution made it extremely useful in all sorts of topical applications—on the skin, in the eye, in the intestine and in the peritoneal cavity. Reduction of the bacterial flora in the intestine became a matter of interest to the physician as well as the surgeon. Infections with resistant organisms became more common, and neomycin proved to have retained its value in many instances. This book covers the microbiologic, bacteriologic and clinical aspects very fully, with a detailed bibliography. The various sections are authoritative and helpful. It is a valuable reference book.

NEUROPATHOLOGY. J. G. Greenfield and others. 640 pp. Illust. Edward Arnold Ltd., London; The Macmillan Company of Canada, Limited, Toronto, 1958. $18.00.

This large and authoritative volume deals systematically with all the known lesions of nervous tissue, with the notable exception of neoplasms. The reason for this exception is that a companion volume on cranial and spinal tumours is in preparation under the editorship of Professor Dorothy S. Russell of the London Hospital.

While a large amount of the book is written by Greenfield, a very satisfying chapter on vascular diseases is contributed by Blackwood. Meyer has a very important section dealing with anoxias, intoxications and metabolic disorders. He also describes the present status of knowledge of the pathology of epilepsy and he has a short chapter on psychoses of obscure pathology. McMenemey contributes an account of the dementias and progressive diseases of the basal ganglia, and Norman gives us a very important chapter summarizing his tremendous experience of malformations of the nervous system, birth injury and diseases of early life.

Greenfield's contributions to the book show his great knowledge of and interest in the history of neuropathology. In all his chapters, however, with the possible exception of that on traumatic lesions of the central and peripheral nervous systems, his subjects are brought up to date and the present state of knowledge is well summarized.

It is a great pleasure to recommend very highly this beautifully produced and well-illustrated book. It will be not only an important working guide but a standard book of reference to neuropathologists and neurological clinicians.

A HISTORY OF TECHNOLOGY. Vol. IV: The Industrial Revolution c.1750 to c.1850. Edited by C. Singer and others. 728 pp. Illust. The Clarendon Press, Oxford; Oxford University Press, Toronto, 1958. $25.50.

The ambitious project of writing a popular history of technology from the earliest times to the present day is nearing completion, and increasing immeasurably in complexity as the twentieth century is approached. The present volume deals with the Industrial Revolution and thus covers the period 1750-1850, a feat possible only by skilful compression. How the period from 1850 on will be compressed into a single and final volume remains to be seen.

Much of the present volume is of course of interest to the general scientist rather than to the physician. The volume begins with some account of farming and fishing techniques, and continues with a section on mining and metallurgy. It is of interest to note that an early safety lamp, without which mining development would have been impossible, was invented by an Irish physician, W. R. Clanny.

In an excellent chapter on the development of power to 1850, Forbes shows how the steam engine slowly displaced other prime movers, such as the windmill (incidentally in 1581, Dutch workmen were protesting against the windmill for fear of unemployment—shades of automation!). Other chapters take us through the early stages of the steam engine and water mill. The tale continues with chapters on the chemical industry, and on gas lighting and heating. Our old friend Stephen Hales of blood pressure fame makes a brief appearance with his experiments on inflammable gas, and various other inquisitive clergymen are given credit for work in this field. The textile industry, ceramics, glass and machine tools are dealt with, before a section is reached which will interest public health workers in particular, for it contains chapters on water supply and sewage disposal, serving to remind us once more of some ever-present unpleasantnesses of the good old days. Most of the rest of the book deals with the history of communications — roads, canals, ships, map-making, telegraphy. Finally, Ubbelohde discusses the early stages of the change-over from craft mystery to scientific technology.

The work is exceedingly well illustrated and furnished with a select bibliography. Those interested in the history of science will welcome it as an indispensable reference volume. It will no doubt be a standard purchase for libraries.

PNEUMOCONIOSIS: Industrial Diseases of the Lung caused by Dust. P. F. Holt, Lecturer in Chemistry, University of Reading, England. 268 pp. Illust. Edward Arnold (Publishers) Ltd., London; The Macmillan Company of Canada Limited, Toronto, 1957. $8.50.

In this useful, compact reference book on pneumoconiosis, the chemistry of the dusts which produce pneumoconiosis is discussed in much detail. It is helpful to be able to find a description of the causes of all the pneumoconioses in one small book. From the point of view of a physician it is disappointing that there are no illustrations of morbid anatomy or roentgenological changes in the lungs. Discussion of changes in pulmonary function is also omitted. It is to be hoped that some inaccuracies will be corrected in a second edition. Nevertheless, the wealth of information in it and the bibliography of 657 references make it a valuable addition to the library of everyone interested in industrial medicine or diseases of the chest.

ELECTRON MICROSCOPIC ATLAS OF NORMAL AND LEUKEMIC HUMAN BLOOD. F. N. Low and J. A. Freeman, Louisiana State University. 347 pp. Illust. McGraw-Hill Company of Canada Limited, Toronto, 1958. $26.25.

To our knowledge this book represents the first attempt to publish an atlas of electron microscopy of human blood. The authors describe in a brief introduction the technique used: it is a method which has since become classical and consists of fixing the material in a solution of buffered osmic acid and coating in acrylic resin so as to obtain ultra-thin slides by means of glass knives. Red cells are eliminated by centrifuging.

The illustrations include about 150 plates of which the first 50 are devoted to normal human blood and the remainder to various forms of leukæmias (granulocytic, myeloblastic, stem cell, lymphocytic, monoblastic). Towards the end of the book approximately ten plates are devoted to plasmacytes and to a few elements of the red series. These figures come from a collection of over 200 electron photomicrographs to which are added for the sake of comparison about 15 photomicrographs obtained by the conventional method. Anyone familiar with the difficulties and the complexities of electronic microtechnique will realize the skill and the amount of work involved in publishing such a book. Photographs are in general well reproduced as regards structural details and contrast. Each plate is clearly labelled with arrows for identification purposes and detailed captions.

This book, as the title implies, is purely descriptive and leaves a number of questions unanswered (identification of certain elements such as the morphology of normal basophils, for instance), but this should not surprise anybody in the present state of our knowledge. Some may find the terminology used in the classification of leukæmias somewhat outdated. As it is, however, it stands as an excellent compendium and should certainly be very useful as a basis for discussion and as a reference book.

The day may not be far off when the electron microscope will become an instrument of routine diagnosis in hospital laboratories. The present atlas will then help the hæmatologist in finding his way in this new field, which may become an important part of the clinical work of tomorrow.

ROENTGEN DIAGNOSIS OF ABDOMINAL TUMORS IN CHILDHOOD. Charles M. Nice, Jr., Alexander R. Margulis and Leo G. Rigler, Department of Radiology, University of Minnesota Medical School, Minneapolis. 74 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1957. $4.50.

This monograph covers the subject of abdominal tumours in childhood quite well. They are classified and discussed as regards their anatomical location in such a way that the radiologist may attempt to make a specific diagnosis or at least list likely differential possibilities.

One chapter deals with roentgen methods of examination, with special reference to the value of plain films with the patient in various positions.

The classification divides masses into four main groups: intraperitoneal masses in the region of the liver; other intraperitoneal masses; renal and adrenal masses; other extraperitoneal masses. Under each heading the various lesions are described and illustrated to bring forth diagnostic features.

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DIABETES AS A WAY OF LIFE. T. S. Danowski, University of Pittsburgh School of Medicine. 177 pp. Illust. Coward-McCann, Inc., New York; Longmans, Green & Co., Toronto, 1957. $4.00.

This book represents the combination of scientist, clinician and seasoned medical practitioner embodied in one person. Dr. Danowski has drawn from all of these sources to write a lucid book which covers all of the important aspects of diabetes mellitus as it concerns the patient.

While diabetes mellitus is replete with controversy, this author has been able to present his material in a forthright manner and still, to a large extent, avoid controversy with his fellow scientists and clinicians. Although primarily intended for the laity, this book could be recommended to the medical profession, because of the extremely complete approach to the patient.

Dr. Danowski is a well-known authority on the subject of diabetes mellitus and he has presented every aspect of the subject in a masterful manner. This book is in every way a superb manual for diabetics.

MECANISMES D'AUTOREPRODUCTION (Mechanisms of Autoreproduction). Present Concepts on Cellular Biology. Edited by J. A. Thomas. 430 pp. Illust. Masson et Cie., Paris, 1957. Fr. 5000.–

Analyser des mécanismes de l'autoreproduction c'est tenter d'élucider des mécanismes fondamentaux de la vie aux divers degrés de complexité structurale. Les progrès récents de nos connaissances justifient déjà des synthèses, même si celles-ci ne représentent que des repères bien vite dépassés. Néanmoins, de ces synthèses partielles et provisoires, se dégage déjà la notion de l'unité des mécanismes généraux. Les mêmes principes fondamentaux qui dirigent le mécanisme de l'autoreproduction des constituants cellulaires normaux comme la chromatine, le nucléole, les mitochondries et les microsomes, gouvernent aussi l'autoreproduction des constituants figurés du cytoplasme. L'étude de ses constituants figurés, distincts par leurs caractères chimiques, sérologiques et génétiques permettra de mieux connaître la physiologie normale de la cellule.

Dans ce volume des Exposés actuels de biologie cellulaire, les auteurs, tous éminents spécialistes, ont fait la synthèse du mécanisme de l'autoreproduction des constituants normaux de la cellule, de la production des anticorps, du mécanisme de l'autoreproduction des particules kappa des paramécies "killer", des chloroplastes chez les Euglènes, du facteur à la fois héréditaire et infectieux, responsable de la sensibilité héréditaire de la mouche Drosophile au gaz carbonique aussi bien que celui de l'autoreproduction des virus des plantes, des bactéries et des animaux. Toutes ces questions sont étudiées dans neuf chapitres différents avec un résumé-introduction écrit par M. André Thomas.

Dans le premier chapitre, M. J. Brochet résume les connaissances actuelles sur la reproduction des principaux constituants de la cellule au repos aussi bien que pendant la division mitotique en insistant sur le rôle du noyau et la régénération après ablation du noyau.

Mme de Deken-Grenson étudie l'autoreproduction des constituants cellulaires qui, s'ils disparaissent, ne sont pas habituellement reformés. Ces particules sont responsables de "l'hérédité générale" liée au cytoplasme, tandis qu'au noyau est attribuée une "hérédité spéciale", mendélienne. La perte ou survie de ces particules dépend de leur capacité dans la compétition pour les substances pouvant assurer leur croissance.

M. L'Héritier soulève la question importante de l'hérédité à la fois contagieuse et cytoplasmique. Il montre que la continuité de l'infection héréditaire n'est pas assurée par la forme infectieuse du virus mais par une forme masquée, intégrée au système génétique des drosophiles. Le virus, dans ce cas, est transmis comme un constituant normal de la cellule.

M. Grabar, dans un article assez court, donne un résumé des hypothèses les plus récentes sur la formation des anticorps.

M. Barbu, après une introduction sur la forme et constitution chimique des virus, explique comment les acides nucléiques et les protéines sont organisés dans le virus. Puis, il continue sur le mécanisme qui est déclanché à partir du moment où un virus touche une cellule hôte jusqu'au moment où les nouveaux virus sont libérés dans le milieu. Dans cet exposé, M. Barbu présente un ensemble des faits et observations choisis pour mettre en évidence le rôle des acides nucléiques, d'une part dans la synthèse des constituants des virus, d'autre part dans l'organisation et le groupement de ces constituants.

M. Limasset passe en revue les dernières acquisitions dans les connaissances de structure des virus des plantes. Relation entre des protéines et l'ARN, et la spécificité fourni par l'ARN de virus. Il explique en plus le comportement des virus chez les insectes vecteurs.

M. René Thomas analyse les mécanismes des transferts génétiques en termes de biochimie à l'échelle macromoléculaire. La lysogénie et l'incorporation de prophage dans le mécanisme génétique des bactéries et le phénomène de transduction où le segment transmis peut comporter toute une série de loci génétiques adjacents, permettent d'introduire la notion d'allélisme à l'échelle macromoléculaire.

Mlle Cateigne analyse les rapports physiologiques entre les virus animaux et cellule hôte. En étudiant chaque stade du cycle viral elle souligne la complexité des virus animaux.

Dans le dernier chapitre, M. Hannoun montre les relations entre l'autoreproduction des virus et le métabolisme des cellules animales infectées. Les virus ne sont que les inducteurs capables de changer le métabolisme cellulaire. On peut retrouver toute la gradation des inducteurs de ceux présents dans la cellule normale, transmis héréditairement sans pouvoir pathogène et non transmis par inoculation, au virus pathogène qui aussi contrôle des synthèses cellulaires mais est transmis par inoculation et possède le pouvoir pathogène, les facteurs de transformation, virus de drosophile, virus latent restant en position intermédiare. Tous ces inducteurs figurés (virus) entrent en concurrence avec les inducteurs normaux.

Dans ce résumé assez court, il est impossible même de mentionner tous les problèmes soulevés dans ce dernier volume des Exposés actuels de biologie cellulaire. Ce livre sera très intéressant pour ceux qui veulent comprendre le mécanisme intime de multiplication virale car la plus grande partie de ce volume est consacrée à l'étude des virus. Mais l'intérêt est encore plus grand pour tout biologiste qui veut connaître le secret de l'autoreproduction de la matière vivante.

HIGH ARTERIAL PRESSURE. F. H. Smirk, University of Otago, Dunedin, New Zealand. 744 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1958. $18.00.

From the introduction to this book one learns that the author first began his studies on "basal" blood pressure in 1936. Out of this work grew his belief that essential hypertension is not due to a single pathological process, and that in some cases simple overactivity of physiological processes may lead to hypertension, whilst in others pathological changes may be the primary cause. Basal blood pressure is, according to the author, "much less variable than the casual blood pressure; indeed in health it is a physiological constant for the individual".

Of the 21 chapters of this treatise more than half are concerned with fundamental questions regarding normal, high, and low blood pressure. There are chapters on the natural history and ecology of high and low blood pressure, influence of living conditions on blood pressure, and the physiology of blood pressure regulation. The racial, geographical and environmental influences are particularly interesting and, to this reviewer, most instructive. They reflect both personal experience in different parts of the world and an unusually extensive knowledge of world literature on the subject. The same broad approach is brought to bear upon the pathogenesis of hypertension in general and of essential hypertension in particular. No dogmatic statements are made but the evidence is presented, followed by the author's own fair and acceptable hypothesis of the etiology and pathogenesis of essential hypertension, which leads one logically to a positive approach in treating this disorder.

Convincing evidence based on extensive personal clinical experience is presented to prove that the outlook of hypertensive patients can be substantially improved by treatment. Treatment by rauwolfia drugs and ganglionic blocking agents, singly and in combination, is described in great detail; the management of side effects receives careful attention. These chapters should be of great help to anyone undertaking to treat hypertensive patients. Experts should appreciate the fair and comprehensive presentation of all the known facts and the suggestions regarding possibilities for future research. As a reference book it is probably unique and will, no doubt, be used by workers in many fields, some only remotely allied to hypertension. A lucid style and good printing contribute greatly to make the reading of this book a pleasurable as well a useful experience.

ELEKTROENCEPHALOGRAPHISCHE STUDIEN BEI HIRNTUMOREN (Electroencephalographic Studies on Cerebral Tumours). Rudolph Hess, University of Zurich. 106 pp. Illust. Georg Thieme Verlag, Stuttgart; Intercontinental Medical Book Corporation, New York, 1958. $4.70.

Hess's study is based on the analysis of the electroencephalographic records of 682 verified and localized brain tumour cases from Krayenbühl's neurosurgical clinic in Zürich. It deals with the relationship between localization and the EEG changes. The different types of diffuse and focal electroencephalographic abnormalities observed are described in detail and correlated with the various tumour sites. It is not concerned with the influence the nature of the tumour and its growth might have on the EEG. The study, however, is not purely statistical. Important practical and theoretical conclusions are offered. The findings of former investigators are discussed and largely confirmed. In some instances older views will have to be modified on the basis of Hess's larger material. In this reviewer's opinion the main value of the present study consists, aside from the extensive material on which it is based, in the extreme caution which the author applies in his conclusions modestly called hypothetical.

THE STORY BEHIND THE WORD: Some Interesting Origins of Medical Terms. H. Wain. 342 pp. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1958. $9.25.

Physicians of all ages must from time to time stop to ponder the origin of some medical terms in current use. Dr. Wain has now gathered together nearly 6000 medical terms in alphabetical order, and written short notes on their origin. The result is a book which will be dipped into by many people for sheer pleasure as well as for information. To start reading it is to risk being drawn further into the study of etymology. Dr. Wain has taken a very wide view of his task, and not only gives us little notes to explain Greek or Latin origins of medical words, but also the significant biographical points in lives of famous scientists whose names have passed into the literature. Thus in ten lines he tells us the origin of Gram's stain and in another ten lines the salient facts about the establishment of the Nobel prizes. We learn that "quack" comes from the low German, "quackelen", "to talk much and idly", and that the word "dope" comes from the Dutch and originally meant the greasing of axles. Inevitably the book contains a great deal of medical history, and would serve equally well as a reference book or as a present for someone interested in words and their origins.

QUANTITATIVE UNTERSUCHUNGEN AN DER SEHRINDE (Quantitative Investigations of the Visual Cortex). Herbert Haug, Erlangen. 130 pp. Illust. Georg Thieme Verlag, Stuttgart; Intercontinental Medical Book Corporation, New York, 1958. $3.60.

By statistical analysis of thousands of histological slides Haug tries to establish a statistically significant relationship between the number and size of neurons and glia cells in the mammalian isocortex and the brain volume and phylogenetic position of the various species investigated. The same method is applied as regards human ontogenesis in embryos and the interindividual variability of adult human brains. Haug also investigates the question whether there are significant differences between the visual cortex of schizophrenics and normal adults. The visual cortex (area 17 of Brodman, O_c of Economo) was chosen because it is easier to compare quantitatively in the phylogenetic scale than other areas of the isocortex. The answers to the above problems are given in a number of quotients and formulæ interesting mainly to neuroanatomists and embryologists. Psychiatrists and neuropathologists will find it interesting to read that the visual cortex of schizophrenics is characterized by a relative increase in the volume of glia nuclei. A positive histological diagnosis cannot be based on this finding in an individual case, but a high quotient of nerve cell to glia cell nuclei would rule out schizophrenia. For the non-specialist reader, the book offers an interesting historical outline on neurohistology and particularly cytoarchitectonic research.

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ABSTRACTS *from current literature*

MEDICINE

Mitral Insufficiency from Ruptured Chordæ Tendineæ Simulating Aortic Stenosis.

P. J. OSMUNDSON, J. A. CALLAHAN AND J. E. EDWARDS: *Proc. Staff Meet. Mayo Clin.*, 33: 235, 1958.

A case of mitral insufficiency resulting from rupture of the mitral chordæ tendineæ in a 24-year-old man is presented. Physical findings simulated those in aortic stenosis, although the aortic valve was found normal at cardiac catheterization and at necropsy. Explanation of this finding is based on the presence of a "jet lesion" on the septal wall of the left atrium near the aortic valve. It is presumed that the regurgitant stream of blood passing through the mitral valve impinged at the site of the "jet lesion" and caused a murmur and thrill. By coincidence, this area was the one normally adjacent to a portion of the aortic valve.

The cause of the ruptured chordæ tendineæ is unknown, but evidence supports the opinion that bacterial endocarditis, later healed, was the underlying factor. S. J. SHANE

Atrial Septal Defect with Mitral Valvulitis: Clinical and Catheterization Diagnosis.

F. A. BASHOUR AND D. H. SIMMONS: *Ann. Int. Med.*, 48: 1194, 1958.

An examination of the clinical and laboratory data, obtained in six proved instances of mitral valvular disease with atrial septal defect, indicates that it is, for practical purposes, impossible to differentiate the ordinary case of this syndrome from simple atrial septal defect. Cardiac fluoroscopy, murmurs, electrocardiogram and the physiological data in these proved instances of Lutembacher's syndrome were in no way different from similar observations in proved instances of isolated atrial septal defect.

The data on pressures, oxygen saturations, the calculated left-to-right shunts and the cardiac outputs fall well within the range of values previously observed in patients with isolated atrial septal defects. It is therefore unlikely that physiological data of any one case of atrial septal defect associated with mitral lesion could be helpful in differentiating it from the isolated atrial septal defect.

Clinically, the differentiation of the two conditions is also difficult. The typical murmurs of mitral disease may be present in purely congenital lesions in the absence of mitral involvement. Furthermore, true mitral murmurs in the presence of a mitral lesion may be minimal or even lacking.

The two conditions cannot be differentiated by radiographic studies of the heart and the pulmonary vasculature. In two cases these findings were indistinguishable from those of simple mitral valve disease.

There are probably only two circumstances under which the diagnosis can be made clinically, short of cardiotomy or autopsy. If calcification of the mitral valve can be observed radiographically in the presence of a proved atrial septal defect, the diagnosis of Lutembacher's syndrome would seem to be well founded. In the absence of calcium, however, the only other way to make the diagnosis would be to measure a gradient across a stenosed mitral valve, either by introducing a catheter through the atrial septal defect and into the left atrium and left ventricle, or by direct left atrial puncture, and then introduction of the catheter into the left ventricle. If a significant gradient can be demonstrated across a stenosed mitral valve under these circumstances, the diagnosis of Lutembacher's syndrome would certainly seem well founded.

For practical purposes, a clinical diagnosis of combined atrial septal defect and mitral valvular disease can never be made with certainty, and for that reason many reported instances without operative or autopsy confirmation must be questioned.

In treatment it has been proved reasonable first to do a mitral valvotomy through the atrial septal defect, and then to repair the defect, provided the mitral valvular lesion is predominantly stenosis. S. J. SHANE

Tuberculosis and Diabetes.

R. A. SCOTT: *Am. Rev. Tuberc.*, 77: 990, 1958.

The mortality rate among diabetic tuberculous patients treated before the advent of antimicrobial therapy was eight times that of the nondiabetic group. In the chemotherapy group, the mortality rate of diabetic tuberculous patients was approximately twice that of the nondiabetic group.

All of the deaths from pulmonary tuberculosis among the diabetic tuberculous patients treated with antimicrobial agents occurred in those who received what is now considered to be ineffective therapy. There were no deaths from active pulmonary tuberculosis among those who received effective chemotherapy.

Tuberculous diabetics who received chemotherapy tolerated major thoracic surgery as well as the nondiabetic group.

From this series it appears justifiable to conclude that the mortality rate from pulmonary tuberculosis of diabetic tuberculous patients who receive adequate chemotherapy should be no greater than that of the nondiabetic tuberculous group. S. J. SHANE

Carcinoma of the Pancreas: A Clinical Study Based on 84 Cases.

D. BIRNBAUM AND J. KLEEBERG: *Ann. Int. Med.*, 48: 1171, 1958.

Clinical and laboratory data of 84 cases of carcinoma of the pancreas in Israel showed that this disease occurred mainly in Jews originating from Europe, and rarely in those from the Orient.

Anorexia and loss of weight were the commonest symptoms, the classical diagnostic syndrome of painless jaundice being rare. Mental symptoms occurred in 10 patients. Only about 50% of the patients with jaundice had a distended gall-bladder.

Increased erythrocyte sedimentation rate was very common. Hyperglycæmia and positive glucose tolerance tests were observed in almost half of the patients, and unrelated to the site of the pancreatic lesion. External pancreatic insufficiency developing in the course of disease was found to be of limited diagnostic value. Radiological examination pointed to the correct diagnosis in 25% of the cases.

The extremely high incidence of thrombo-embolic phenomena, especially in carcinoma of the body and tail of the pancreas, is stressed as an important sign, and the role of trypsin in the thrombo-embolic process is discussed. S. J. SHANE

(Continued on page 694)

Another clinical evaluation of Mio-Pressin* in hypertension

Salient observations:

- "Since hypertension may be caused by a variety of factors influencing several body mechanisms, it is generally believed that a combination of drugs, each having a different site of action, is more likely to be effective than any one drug alone."

- "Eighty-nine per cent of the patients [in this evaluation] had become normotensive by the conclusion of the study."

Smith, C.W., and Thomas, C.G.:
Am. Pract. & Digest Treat.
8:920 (June) 1957.

'Mio-Pressin'—a balanced combination of rauwolfia, protoveratrine and Dibenzyline*—for moderately severe to severe hypertension, in two dosage strengths: No. 2 (standard strength) and No. 1 (half strength).

Smith Kline & French • Montreal 9

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*Reg. Can. T. M. Off.

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(Continued from page 692)

SURGERY

The Management of Acute Cholecystitis.
A. E. LEE: *Brit. J. Surg.*, 45: 523, 1958.

Biliary tract disease is very common in Australia, and in one year 691 patients were treated in Brisbane Hospital, with 17 deaths. The usual course of gall-bladder disease is believed to start with the primary gallstone and develop acute cholecystitis or mucocele due to obstruction by a stone, then secondary gall-stones, repair after acute cholecystitis, and finally stones in common or hepatic ducts and stenosis of the duct system. These conditions produce biliary colic, acute cholecystitis and ductal destruction. It is claimed that so-called chronic cholecystitis rarely causes any symptoms, the dyspepsia attributed to this lesion being due to anxiety or doctor-induced.

Since it is demonstrable that the average age at death of people with gallstones is above that of the general population, an aggressive surgical attitude towards the possession of gallstones is not advocated. The inflamed gall-bladder is always walled off in all but the aged. Only in the elderly is early surgical intervention to be seriously considered for acute cholecystitis. Then drainage only is indicated as an emergency procedure on a feeble old patient.

The general application of conservative management to the vast majority of cases of acute cholecystitis has resulted in a recovery rate of over 98%. Non-neoplastic disease of the biliary tract is regarded as a nuisance to the possessor rather than a serious threat to life. Surgery of the gall-bladder should be considered as a therapy of pain rather than as a treatment for gallstones.

BURNS PLEWES

Regression After Open Valvotomy of Infundibular Stenosis Accompanying Severe Valvular Pulmonic Stenosis.
M. A. ENGLE *et al.*: *Circulation*, 17: 862, 1958.

Three patients with severe valvular pulmonic stenosis had a right ventricular systolic pressure greater than 100 mm. Hg after open valvulotomy performed under hypothermia. The remaining obstruction was localized by pressure measurements to the infundibulum. Surgical exploration of this chamber indicated that the obstruction was not rigid but was due to contraction of the hypertrophied muscle. In the 6 to 20 post-operative months, electrocardiographic signs of right ventricular hypertrophy disappeared, and cardiac catheterization 10 to 15 months after operation disclosed pressures within normal limits in the right ventricle, with only slight or no transvalvular gradients.

Severe valvular stenosis was apparently responsible for marked hypertrophy of the wall of the right ventricle, sufficient by itself to narrow the infundibulum once the obstruction at the valve was relieved. Restoration of valve function by valvuloplasty reduced the work of the ventricle so that the hypertrophied myocardial fibres returned to a more nearly normal size, and was accompanied by complete regression of this secondary form of infundibular stenosis.

It is implicit in these observations that if the valve has been opened fully and there is no fixed obstruction, such as a diaphragm or ring within the right ventricle, additional attempts to treat the muscular stenosis surgically are unnecessary.

S. J. SHANE

Reconstruction Versus Prosthesis.
J. J. CALLAHAN: *A.M.A. Arch. Surg.*, 76: 737, 1958.

Reasons are given for preferring a reconstruction of the hip to a prosthesis for femoral neck fractures in aged patients in certain cases: (1) non-union of the neck of the femur with absorption of the neck; (2) aseptic necrosis of the head; (3) severe osteoarthritic changes; (4) in the presence of malformations; (5) subcapital fractures. The advantages of early weight-bearing, allaying the patient's anxieties, and relief of pain are great. The disadvantages of Trendelenburg gait, restriction of flexion and shortening are minor.

Insertion of hip prostheses in the young is opposed because failure of treatment precludes successful alternatives, available prostheses are too limited in sizes, postoperative pain from sclerosis is intractable, removal of prosthesis results in too great a shortening, plastic heads may fracture, and metal has problems of sensitivity.

Replacement prosthesis may be utilized when the patient is past life expectancy, or in true subcapital fractures, and may be useful in pathological fractures or when the fracture occurs in a patient with malignancy elsewhere.

BURNS PLEWES

Arterial Repair During the Korean War.
C. W. HUGHES: *Ann. Surg.*, 147: 555, 1958.

There have been duplications in reports of the repair of major arteries in the U.S. Army in Korea, and this reports on all 304 cases operated upon. The care of such cases finally adopted emphasizes the importance of resuscitation, rapid evacuation to a hospital, delayed closure of the debrided wound after arterial repair, delayed repair of tendons and nerves, fasciotomies for swelling, bivalving of plaster casts applied. Sympathetic blocks and sympathectomies were often done as well.

Ligation of the subclavian, axillary, brachial, femoral or popliteal arteries resulted in about the same amputation rate (51%) as was reported after World War II. But great improvement was achieved by surgical repair of these arteries in Korea in the 269 cases attempted (13%). The best method of repair of a severed artery was by anastomosis. Next best was by autogenous vein graft, and the poorest method was by artery homograft. Undoubtedly, better results followed in cases in which arterial repair could be done within 10 hours.

BURNS PLEWES

THERAPEUTICS

New Effective Method of Nebulizing Bronchodilator Aerosols: Clinical and Physiological Effects.
G. J. BECK: *Dis. Chest*, 33: 607, 1958.

The gas phase of dichlorodifluoromethane is a well tolerated and expedient propellant for use in the nebulization of bronchodilator aerosols. Inhalation in concentrations of approximately 4% in patients with bronchospasm from a compact pressure apparatus produced no change in vital capacity. Side reactions from the inhalation of these low concentrations of dichlorodifluoromethane were minimal and uncommon.

Studies of the effect of 0.5% isoproterenol hydrochloride and 2.25% racemic epinephrine when inhaled in the form of an aerosol by means of a gas

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phase of dichlorodifluoromethane-propelled nebulizer revealed clinical relief of dyspnœa and corresponding increases in vital capacity. Side reactions to these bronchodilators were rare and confined to tremulousness and tachycardia. Reduction in the amount of drug inhaled reduced their incidence. The use of the bronchodilator solution in which 0.4% isoproterenol sulfate was combined with 2.0% phenylephrine was not followed in this series by either tremulousness or tachycardia. Neither drug caused change in the blood pressure of normotensive or hypertensive patients when nebulized with this type of device. S. J. SHANE

PATHOLOGY

Fatal Toxic Hepatitis Following Chlorpromazine Therapy. Report of a Case with Autopsy Findings.

A. E. RODIN AND D. M. ROBERTSON: *A.M.A. Arch. Path.*, 66: 170, 1958.

Jaundice is a common manifestation of untoward reactions to chlorpromazine therapy. It has been reported in 0.2% to 8% of cases treated with this drug. Only two persons have been reported to have died from this reaction; the authors present a third case from the Kingston General Hospital. Both liver biopsy and autopsy findings are described in detail. The jaundice developed 22 days after the onset of chlorpromazine therapy, which lasted only nine days with a total dose of 1800 mg. of the drug. The patient showed the clinical picture of obstructive jaundice, and a laparotomy was performed on the 24th day of illness. No obstruction was found and the liver biopsy revealed centrilobular bile thrombi. On the 40th day of disease the patient died in a state of shock. At autopsy the liver showed more marked degenerative changes than in the biopsy specimen, with marked necrosis of hepatic cells in the central half of all lobules.

The authors stress the similarity of the findings in this case with those of the other reported cases and with the changes observed in early obstructive jaundice, and jaundice due to arsphenamine, thiouracil and methyltestosterone. W. GROBIN

ORTHOPÆDICS

Dupuytren's Contracture.

R. D. LARSEN AND J. L. POSCH: *J. Bone & Joint Surg.*, 40A:773, 1958.

In keeping with other series, Dupuytren's contracture was noted by these authors to be more common in the right hand and more commonly bilateral than unilateral. A single nodule in the skin in line with the ring finger and most often at the distal palmar crease is the earliest manifestation. More nodules appear which gradually become organized into one or more contracted longitudinal bands. The metacarpophalangeal and proximal interphalangeal joints are drawn into flexion, but not the distal interphalangeal. In keeping with the work of Kanavel, Koch and Mason, these authors found that Dupuytren's contracture was more apt to occur in patients who did not perform manual labour.

Today there is general agreement that the disease involves the palmar fascia, although some consider that this fascia is secondarily involved in an inflammatory process which arises in the interstitial tissues

of the hand. The pretendinous bands of the palmar fascia pass into the superficial digital fascia. These fascial fibres passing from the palm into the fingers ultimately attach to the sides of the proximal and middle phalanges. Kaplan concluded that the flexion contracture of the phalanges in Dupuytren's contracture depended upon the contracture of the phalangeal insertion of the pretendinous bands.

There are four major concepts concerning the histopathology of Dupuytren's contracture: (1) benign hyperplasia of the fibrous tissue arising in the palmar aponeurosis; (2) inflammatory changes arising in the interstitial connective tissue of the palm and secondarily involving the aponeurosis; (3) benign neoplasm-fibroma; and (4) cellular hyperplasia in response to rupture of the collagenous fibres of the palmar aponeurosis.

These authors conclude that the pathological changes consist of active proliferation of fibroblasts in intimate association with numerous thick-walled vessels associated with increased capillary vascularity. The proliferating tissue forms non-encapsulated nodules of varying size within the aponeurosis. Changes proceed from young, cellular, immature fibrous tissue into mature, contracted, dense, collagenous tissue. As maturation progresses, the vascularity decreases.

Non-operative treatment of Dupuytren's contracture with local injections of pepsin, fat solutions, fibrolysin, copper sulphate and pancreatic extract is of little value. Cortisone was also found to have no effect upon the disease. This study would suggest that alpha-tocopherol might lead to a temporary softening of the contracture, but the progressive course of the disease was not altered.

Although most authorities agree that operative treatment is the only choice in the majority of cases, there is some question about the type of operation. Fasciotomy of the contracted bands, either blindly or under direct vision, is the simplest procedure. A limited or partial fasciectomy of the diseased fascia, with varying degrees of excision of normal fascia, is the next simplest. In other cases radical excision of all recognizable palmar fascia together with vertical septa which pass to the pre-osseous fascia and the pretendinous bands extending into the fingers is carried out. When to operate, and whether or not to operate on a patient with the earlier stages of the disease, pose a difficult problem. If the contracture is progressing rapidly, operation is recommended; if it remains stationary, and the contracture is in the earlier stages, surgery is not required.

Fasciotomy has been advocated as a preliminary operation in severe cases to allow gradual stretching of the tissues in preparation for more radical procedures. In these operations the importance of preserving the small vessels, which penetrate the fascia from below and supply the skin, is stressed. After the subcutaneous fat is dissected away from the palmar fascia as far distally and proximally as possible, the fascia is divided transversely in the proximal portion of the palm. It is not considered necessary to reach the insertion of the palmaris longus, since the most proximal portion of the fascia is rarely involved in the disease. With proper choice of operation and careful attention to operative details, excellent or good results can be expected in between 80 and 90% of patients operated upon.

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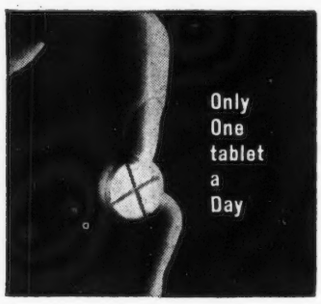

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references:
1. Grieble, H.G., and Jackson, G.G.: Prolonged Treatment of Urinary-Tract Infections with Sulfamethoxypyridazine. *New England J. Med.* 258:1-7, 1958.
2. Editorial: *New England J. Med.* 258:48-49, 1958.

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AWARDS FROM THE ALLERGY FOUNDATION OF AMERICA

The Allergy Foundation of America announces awards of $500 summer or quarterly scholarships to 22 medical students from medical schools throughout the U.S. and Canada to encourage young students to broaden their knowledge in the field of the allergic diseases by research and clinical training. The purpose of these awards is to afford the students experience in the basic sciences related to allergy and consolidate the application of this knowledge through clinical experience. These summer scholars will work under the direction of outstanding scientists both in research and in the clinics.

Selected this year were Mr. A. P. Naimark of McGill University, Mr. E. M. Dundas of the University of Western Ontario and Mr. L. A. Moroz of the University of Manitoba. These students were nominated by the deans of their respective medical schools in collaboration with the heads of basic science departments of these institutions.

Further information about these awards may be secured from Dr. Charles D. Marple, Director, Allergy Foundation of America, 801 Second Avenue, New York 17, N.Y.

THE WILLIAM OSLER MEDAL

The William Osler Medal of the American Association for the History of Medicine is awarded annually for the best unpublished essay on a medico-historical subject written by a student in one of the medical schools of the United States or Canada.

Essays submitted should not exceed 10,000 words in length, and should demonstrate either original research or an unusual understanding of a medico-historical problem. It is expected that the student will seek help only from faculty advisers, and from sources open to all investigators, such as libraries and museums. The prize-winning essay may be considered for publication in the *Bulletin of the History of Medicine*, which is the

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official organ of the Association. All students are eligible and may submit essays at any time up to the next entry date after graduation. The next entry date terminates April 1, 1959. Essays should be submitted to: Dr. Samuel X. Radbill, 7043 Elmwood Avenue, Philadelphia 42, Pa.

PRIZE ESSAY CONTEST

The American College of Chest Physicians is offering three cash awards to winners of the 1959 prize essay contest. First prize is $500, second $300 and third $200. The contest is opened to undergraduate medical students throughout the world. Essays may be written on any phase of the diagnosis or treatment of chest diseases (cardiovascular or pulmonary). The contest closes on April 15, 1959. Further information may be obtained from: American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois, U.S.A.

WELDERS' LUNGS

Harding, Mclaughlin and Doig review the literature on the subject of lung changes in welders since 1936 and recall that there was general agreement that, although welders' chest radiographs present characteristic appearances, there is little or no disability due to these changes, and that iron oxide alone does not cause fibrosis of the lungs (*Lancet*, 2: 394, 1958).

Newer methods of welding have changed the composition of the fumes given off during the process, and they now contain much less iron oxide and include silicates and the oxides of titanium, manganese and calcium. One of the authors with his collaborators has previously described the presence of well-marked silicotic nodules in the lung of a carbon-arc welder, and fibrosis of lungs as well as emphysema with loss of elasticity was found in other cases and related to the presence of iron oxide. The present report gives details of four electric-arc welders and one oxyacetylene cutter who came to necropsy. In the first case pneumoconiosis was present at the age of 69, but the authors did not consider that there was sufficient fibrosis to produce any disability or to play any part in his death. In the second case there was no fibrosis after more than 40 years of welding; in the third case there was insignificant fibrosis after more than 30 years' welding, and in the fourth case slight though definite mixed-dust fibrosis was present after 28 years of arc welding, mostly in enclosed spaces. Chronic bronchitis and emphysema were considered the main cause of his death and were possibly occupational in origin, but may have originated earlier in life. The fifth case was that of an oxyacetylene cutter who had been at this work for a total of nine years. No fibrosis was found in his lungs.

The authors consider that it is established beyond doubt that considerable quantities of pure iron oxide can be inhaled and remain in the lungs without producing fibrosis. The slight degrees of

fibrosis found in the lungs of some electric-arc welders are caused by other constituents of the welding fumes or possibly by some of the gases evolved. Only when extraneous sources of silica, such as are present in fettling-shops of foundries, are inhaled by the welders, will they develop more severe forms of fibrosis amounting in some cases to mixed-dust pneumoconiosis and resulting occasionally in disabling disease.

BOOKLET FOR TEENAGERS

The American Heart Association has recently published a booklet entitled "Decision for Research" as a part of the Heart Association campaign to recruit many more "young, capable, energetic minds" for research in the medical and biological sciences. The booklet is designed to help science-minded teenagers decide whether or not they wish to enter the career of a medical research worker. Helpful hints are offered to those who decide in the affirmative, showing the recommended progress of a research-minded student through high school, college, graduate or medical school. The booklet also contains a listing of sources of information on scholarships, career guidance and ideas for student science projects. Although directed mostly at American youth, the booklet could serve a most useful purpose in Canada. Copies are available from The National Heart Foundation, 501 Yonge Street, Toronto 5, Ont.

RESEARCH IN RADIOLOGY

The National Research Council has recently announced the winners of the James Picker Foundation awards for research on radiological methods, both diagnostic and therapeutic. The three Canadian grants went to Dr. Albert Jutras, Department of Radiology, Hôtel-Dieu Hospital, Montreal, for work on "Fibroplastic infiltration of the submucosa in minute cancers of the stomach and its effects upon gastric motility and radiological images"; Dr. J. S. Dunbar, of the Montreal Children's Hospital, for work on "Effects of barium sulfate on the tracheo-bronchial tree of rats in comparison with other contrast media"; and to Dr. R. L. de C. H. Saunders, of the Department of Anatomy, Dalhousie University, Halifax, N.S., for "X-ray microscope studies of the nervous system with special reference to the blood supply of the cerebral cortex and spinal cord".

RESEARCH ON THE PROBLEMS OF AGEING

The Ciba Foundation in London, England, has organized a fifth and final competition for the year 1959 on the theme of "Basic Research Relevant to the Problems of Ageing". Approximately five awards of an average of £300 each are being offered. The work submitted may be unpublished, may have been published in 1958 or may be under consideration for publication. Before an entry is submitted, copies of the regulations and form of application must be obtained from: The Director, The Ciba Foundation, 41 Portland Place,

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London, W.1, and entries must not be received later than January 10, 1959.

INTRACRANIAL ANEURYSM IN THE GERIATRIC PATIENT

The number of authenticated intracranial aneurysms in people over 70 is very small. Smolik and Nash (*J. A. M. A.*, 167: 931, 1958) demonstrated the presence of such lesions in three patients aged 66, 77, and 78 respectively. Arteriography was well tolerated under thiopental anæsthesia with 50% diatrizoate as contrast medium. Because of pain or progressive neurological deficit all three patients underwent ligation of the common carotid on the side of the aneurysm. In two patients the operation was successful and relief of pain and improvement of function were obtained. The third patient developed hemiparesis eight hours after clamping and died 30 days later in spite of immediate release of the clamp. The authors believe that such lesions will be encountered with increasing frequency in the elderly.

THE REACTION TIME IN MYXŒDEMA

A method for measuring accurately the reaction time is described by Murray (*Lancet*, 2: 384, 1958), and the circuit of the apparatus used for these measurements is shown in a diagram. A group of 50 patients with hypothyroidism was studied, and 101 healthy people and 10 patients with normal thyroid function with anæmia from various causes (hæmoglobin less than 60%) were used as controls. The normal ranges in each age group were found to be significantly shorter than in the myxœdematous patients of the same age group. During therapy with thyroxine the reaction times of the myxœdematous patients decreased and when they became euthyroid lay within the normal ranges in 23 out of 25 patients. This improvement in reaction time paralleled the changes in B.M.R. and serum-cholesterol levels. Administration of dexamphetamine sulfate decreased the reaction time in both healthy people and myxœdematous patients, but the decrease was greater and more prolonged in the latter. The author discusses the advantages of this method for diagnosis of suspected hypothyroidism and for assessment of response of therapy over the other methods. The apparatus is portable and inexpensive, and permits considerable accuracy in timing. Furthermore, it causes minimal inconvenience to the patient.

A NEW JOURNAL ON NEUROSURGERY

The well-known German publishers, the Georg Thieme Verlag of Stuttgart, West Germany, have announced the appearance of a new periodical, *Neurochirurgia*, which will publish original articles in English, French or German, with a summary in the other two languages, as well as general surveys of current problems and reviews of important original work. Its list of collaborators includes several well-known Montreal neurosurgeons. It will appear twice a year and the price of each copy is 18 DM.

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EFFECT OF KANAMYCIN ON MYCOBACTERIUM TUBERCULOSIS IN VITRO

Kanamycin is a new basic water-soluble antimicrobial derived from *Streptomyces kanamyceticus*. It appears to be effective against tubercle bacilli *in vitro* and has been shown to exert a marked suppressive effect on experimental tuberculosis in guinea pigs and mice. Patnode and Hudgins (*Am. Rev. Tuberc.*, 78: 138, 1958) confirm and extend these observations, through the use of a synthetic liquid medium with and without bovine albumin or human serum. Virulent and attenuated strains of tubercle bacilli were used, and their susceptibility to kanamycin was determined in a modified Proskauer and Beck synthetic liquid medium.

Under the experimental conditions described, kanamycin appeared to be highly active against *Mycobacterium tuberculosis in vitro*. With H37Rv (human) tubercle bacilli, the concentration of drug required for complete bacteriostasis was determined to some extent by the composition of the medium (presence or absence of albumin or serum) and the incubation period.

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TRANSAMINASE ACTIVITY IN GASTROENTEROLOGY

Two recent papers in *Lancet* (1: 1245 and 1249, 1958) deal with transaminase determination in relation to liver disease.

Serial estimation of glutamic oxaloacetic transaminase was performed in plasma of ten patients with chronic liver disease by O'Brien and his colleagues and enabled them to follow the effects of cortisone therapy in these patients. Dramatic fall of the plasma glutamic oxaloacetic transaminase level (P.G.O.T.) was observed within 48 hours in 3 of the 5 patients with active chronic hepatitis. In a fourth case the fall was more gradual but the general pattern of improvement was the same. In the fifth case the fall was equivocal after a fourfold increase in dosage of cortisone. In the other five patients with chronic liver disease of different etiology there was no significant fall in P.G.O.T. after cortisone treatment. The authors conclude that their study indicates that cortisone administration reduced the rate of liver-cell necrosis in relapses of chronic active hepatitis.

Another investigation by Pryse-Davies and Wilkinson was done in order to establish whether serum transaminase activity should be recommended for inclusion in the routine liver function tests in a hospital laboratory. More than 1000 determinations were made on 226 patients and 50 healthy controls; 66 patients had ulcerative colitis, 13 obstructive jaundice, 15 infective hepatitis, 27 cirrhosis or chronic hepatitis, 27 hepatic metastases, 11 cholecystitis, 35 miscellaneous diseases of the intestinal tract not involving the liver, and 25 no organic disease. The methods used for serum glutamic oxaloace-

tic transaminase (S.G.O.T.) and for serum glutamic pyruvic transaminase (S.G.P.T.) determinations are described. The authors suggest that values over 40 S.G.O.T. units per ml. and 30 S.G.P.T. units per ml. be regarded as abnormal with their technique.

High values (over 500 units per ml.) for both enzymes are characteristic of infective hepatitis and carbon tetrachloride poisoning. In obstructive jaundice, glandular-fever hepatitis, and toxic hepatitis other than that due to carbon tetrachloride the rise was less marked (100-300 units per ml.). In myocardial infarction S.G.O.T. showed a rise up to 300 units per ml. but this was transient and in addition the S.G.P.T. level usually remained normal. The results in cirrhosis of the liver and carcinomatous metastases were variable, 64% having raised S.G.O.T. values but only 40% raised S.G.P.T. values. The conclusion reached is that addition of transaminase determination to other liver-function tests was extremely useful.

ST. JOSEPH'S HOSPITAL

St. Joseph's Hospital, Toronto, plans to hold its Third Annual Clinical Day on October 29, 1958, with registration to begin at 9.00 a.m. A comprehensive program of lectures is planned which will be of particular interest to general practitioners. The Medical Staff extends a welcome to all interested physicians. Lunch will be served.

SURGICAL TREATMENT OF TETRALOGY OF FALLOT

Results obtained in the surgical treatment of 4062 cases of the tetralogy of Fallot have been analyzed by 39 members of the advisory committee of the Section on Cardiovascular Surgery of the American College of Chest Physicians (*Dis. Chest*, 34: 103, 1958).

Although "good" results were reported in approximately 80% of the patients surviving the various standard operations, patients submitting to these procedures are actually faced with a 39% risk of death or a "poor" clinical result. Complete open repair using cardiac by-pass techniques was reported by some as providing "good" results in most instances, with a total associated mortality rate approaching that of the standard incomplete techniques.

The operative mortality rate associated with open techniques, as reported by most surgeons, was 95%. This indicates clearly that extreme caution should be exercised before any individual or group of individuals embarks upon the development and clinical employment of one of the cardiac by-pass techniques, and also indicates that the total number of these units in any geographic area should be kept as small as is practicable.

In view of the evidence at hand, it would seem advisable to postpone all types of surgery in patients with the tetralogy of Fallot whose general condition is not poor or deteriorating, unless a safe facility for cardiac by-pass and total correction of all the defects is available. If the patient's general

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clinical condition is poor or deteriorating, cardiac by-pass with complete correction of the defects should be done if safe facilities are available, but if not, one of the standard incomplete operations should be performed.

DEMONSTRATION OF THE CARRIER STATE IN CHRISTMAS DISEASE

A slight modification of the thromboplastin generation test was used by Firkin (*M. J. Australia*, 1: 557, 1958) to examine sera from 10 normal individuals, three patients with severe liver disease, five Christmas disease carriers and two true carriers of hæmophilia. Although three of the carriers of Christmas disease had normal results of routine thromboplastin generation tests, the present modification disclosed subnormal levels of Christmas factor in all three. In two of the three patients with liver disease, the Christmas factor was also found to be diminished whereas the two patients who were true hæmophilia carriers were found to have a normal ability to correct the defect in the serum of the patient with Christmas disease.

The author believes that, if this finding of diminution of Christmas factor should apply to all Christmas disease carriers, it will be possible to remove doubts from the female members of these families regarding their having the disease or passing it on to their offspring.

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CORONARY HEART DISEASE IN FORMER FOOTBALL PLAYERS

A study was undertaken by Pomeroy and White (*J. A. M. A.*, 167: 711, 1958) to elucidate the relationship of various environmental factors to coronary heart disease in a group of individuals of the mesomorphic body type. The records of Harvard College alumni disclosed that 424 men had distinguished themselves at football in the years 1901-1930 inclusive. Of these, information was obtained about 355 persons, of whom 34 are known to have or to have had definite coronary heart disease. Because of inadequacy of data the mortality in this group as compared with healthy males of the same age in the general population could not be determined. When comparing the football players with a history of coronary heart disease with those without such a history, the most significant finding was the apparent protection afforded the men by the continuation of a program of heavy exercise. No individual who maintained a heavy exercise program developed coronary heart disease, and even those with moderate exercise were less prone to it.

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MEDICAL NEWS *in brief*

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smoking in the coronary heart disease group, but other factors such as family status and alcohol had no apparent influence. Dietary habits could not be evaluated because of lack of accurate information. The authors believe that a study such as this suffers from the defect that most of the persons under study lead a similar life. A study of racial groups of which certain members live very differently from the others could be more instructive.

TREATMENT OF ALLERGIC RESPONSE TO PENICILLIN

Various manifestations of allergy to penicillin were encountered by Warren (*J. A. M. A.*, 167: 708, 1958) in 10 patients. Pabalate tablets consisting of 300 mg. of potassium salicylate, 300 mg. sodium p-aminobenzoate and 50 mg. ascorbic acid, given four times daily completely relieved the allergic symptoms in less than 48 hours in nine patients. In the tenth patient, who was known to be allergic to penicillin, administration of Pabalate prevented an allergic response to the same preparation to which she had previously reacted with severe urticaria and erythema. The author believes that this treatment warrants further investigation.

HEART SCARE, HEART SURVEYS, AND IATROGENIC HEART DISEASE

In the course of a special heart survey an unusual opportunity arose to study the effects of the suggestion that heart disease might be present in a large number of adults. Of a total of 1154 such persons, 162 were interviewed and their answers recorded to 33 questions listed on a mimeographed form. The results and analysis of these questionnaires form the main part of a report by Wheeler *et al.* (*J. A. M. A.*, 167: 1096, 1958). The authors conclude that, although the suggestion that a person might have heart disease upset and frightened almost half of the people under review, it did not lead to symptoms of heart disease, neurocirculatory asthenia or neuro-

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Vitamin A	4,000 I. U.	Stomach Mucosa	5 mg.
Vitamin D	400 I. U.	Fluorine (CaF_2)	0.015 mg.
Thiamine Mononitrate (B_1)	3 mg.	Copper (CuO)	0.15 mg.
Pyridoxine (B_6)	1 mg.	Iodine (KI)	0.01 mg.
Niacinamide	10 mg.	Potassium (K_2SO_4)	0.835 mg.
Riboflavin (B_2)	2 mg.	Manganese (MnO_2)	0.05 mg.
Vitamin B_{12}	2 mcgm.	Magnesium (MgO)	0.15 mg.
Ascorbic Acid (C)	50 mg.	Molybdenum ($Na_2MoO_4.2H_2O$)	0.025 mg.
Vitamin K (Menadione)	0.5 mg.	Zinc (ZnO)	0.085 mg.
Folic Acid	1 mg.	Calcium (as Carbonate)	230 mg.
Iron (as Fumarate)	30 mg.		

in the picture... during pregnancy

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sis in general in those previously free of such symptoms. A few patients with neurocirculatory asthenia or angina pectoris showed aggravation of symptoms due to those conditions. It is advisable to observe certain rules in order to avoid upsetting people in similar surveys in the future. The patient should be examined soon after his attention has been drawn to the possibility of heart disease being present. Reassurance should be definite and no information should be mysterious or evasive. Unnecessary information about symptoms of disease should not be given to the general public.

CANADIAN CANCER SOCIETY FELLOWSHIPS THE JOHN S. McEACHERN MEMORIAL FELLOWSHIPS

Applicants for these Fellowships shall be graduates in medicine of an approved Faculty of Medicine or hold an advanced degree in physics from an approved Faculty of Graduate Studies; and (a) shall have already pursued postgraduate study in a field related to the diagnosis or treatment of cancer; (b) shall be endorsed by one of the Faculties of Medicine in Canada in order to augment the clinical anti-cancer program in the geographic area of its major influence; (c) shall under this Fellowship pursue further postgraduate study related to the diagnosis or treatment of cancer acceptable to the Advisory Committee on Fellowships of the Canadian Cancer Society; and (d) shall express a firm interest and assume the moral obligation to return to practise their profession subsequently in Canada with a particular interest in cancer, preferably in the sphere of influence of the endorsing Faculty of Medicine.

These Fellowships have an approximate value of $10.00 a day and are tenable for a maximum period of one year. An additional award at the rate of $400 per annum will be made to married Fellows. At the discretion of the Advisory Committee on Fellowships additional amounts may be made available for travelling expenses. Application forms may be obtained through the Dean of the respective Faculty of Medicine from the Canadian Cancer Society, 800 Bay Street, Toronto 5, Ont.

EXPERT COMMITTEE ON WATER FLUORIDATION

The WHO Expert Committee on Water Fluoridation reports* on prevention of dental caries by fluorides, on the basis of experiments carried out in recent years both amongst population groups and in laboratories.

In the United States, 32 million people drink fluoridated water. Fifteen other countries have already undertaken the controlled fluoridation of water supplies. After thorough examination of studies on the biological action of fluorine on the cells and organs (hard tissues, kidney, thyroid, teguments), and on its metabolism (absorption, distribution, storage, excretion), the Committee asserts

*First Report. World Health Organization: Technical Report Series, 1958, No. 146; 25 pages. Price 30 cents.

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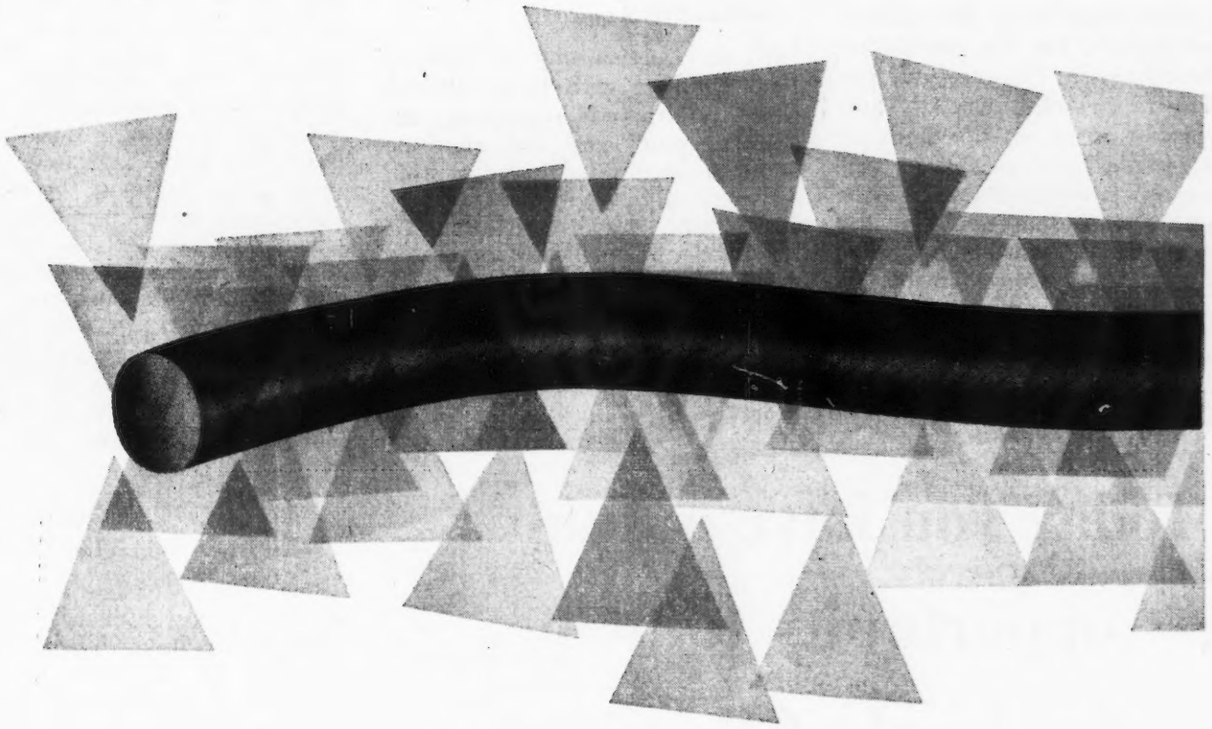

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that fluorides are perfectly harmless when ingested at the optimal concentrations for the prevention of dental caries, i.e., one part per million in drinking water. Their favourable action on the teeth, at all ages, has been proved.

The report concludes with technological considerations on the fluoridation of water and with mention of alternative means of ensuring an intake of fluorine.

RECURRENT ABDOMINAL PAIN: A FIELD SURVEY OF 1000 SCHOOL CHILDREN

In an English city, a total of 1000 children with their mothers were questioned regarding abdominal pain, and 108 of these children were found to suffer from recurrent abdominal pain (Apley and Naish, *Arch. Dis. Child.*, 33: 165, 1958). Disturbances associated with the pain in more than 22% of cases were pallor, vomiting, headache and subsequent sleepiness or lethargy. When compared with 312 controls, i.e. children who were of the same age and sex distribution, several significant differences were recorded. In the children with abdominal pain, there was a considerably higher incidence of a family history of abdominal pain, migraine, peptic ulcer and nervous breakdown. They had more frequent headaches and bilious attacks, and were more often highly strung, fussy and excitable or else anxious, timid and apprehensive than the children without pain. Encephalograms were done on most of the children in both groups and showed no significant differences.

POSTGRADUATE COURSE IN MEDICAL BACTERIOLOGY

The University of Toronto announces a postgraduate course of instruction in medical bacteriology, the first of its kind in North America. A substantial Federal-Provincial health grant has assisted in setting up the course, to be given in the School of Hygiene. The course, to be supervised by Dr. A. J. Rhodes, the School's director, will prepare graduates for the Diploma in Bacteriology.

The new course will provide postgraduate training for physicians and scientists to work in hospital, university, and public health laboratories. Graduates enrolled in the course now starting come from laboratories in Newfoundland, Nova Scotia, Quebec, Ontario, and Saskatchewan, and from Thailand and Ecuador.

SCHOLARSHIPS IN NEUROMUSCULAR DISORDERS

The Sister Elizabeth Kenny Foundation announces continuation of its program of post-doctoral scholarships to promote work in the field of neuromuscular diseases. These scholarships are designed for scientists at or near the end of their fellowship training, in either basic or clinical fields concerned with the broad problem of the neuromuscular diseases.

The Kenny Foundation Scholars will be appointed annually. Each grant will provide a stipend for a five-year period at the rate of $5000

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to $7000 a year, depending upon the scholar's qualifications. Candidates from medical schools in the United States and Canada are eligible.

Inquiries regarding details of the program should be addressed to: Dr. E. J. Huenekens, Medical Director, Sister Elizabeth Kenny Foundation, Inc., 2400 Foshay Tower, Minneapolis 2, Minn.

FELLOWSHIP IN NEOPLASIA

The Memorial Center for Cancer and Allied Diseases, New York, a training centre affiliated with Cornell University Medical College, is offering a special fellowship in medical neoplasia. Its aim is to offer a physician trained in internal medicine the opportunities available at the Memorial Center to study the natural history, diagnosis, complications, pathogenesis, pathology and treatment of cancer, with particular emphasis on the leukæmias, lymphomas and allied diseases. The Fellow will also undertake an active supervised clinical investigation in the field of medical neoplasia. Medical neoplasia is defined as the field dealing with non-surgical cancer and palliative therapy of patients with malignant tumours. Candidates must be graduates of a recognized A.M.A.-approved medical school and must have completed or be completing two years of postgraduate training in internal medicine. The stipend is $6000 per annum, the fellowship for one year with possible renewal. Applications to: Lloyd F. Craver, M.D., Chief, Medical Neoplasia Service, Memorial Center for Cancer and Allied Diseases, 444 E. 68th Street, New York 21, N.Y.

THIRTEENTH INTERNATIONAL CONGRESS ON OCCUPATIONAL HEALTH

The 13th International Congress on Occupational Health will be held in New York City during July 1960. Its theme will be prevention of occupational injury and disease. In particular, the newer occupational hazards such as those

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from radioactive materials will be discussed.

It is expected that several thousand physicians, nurses, industrial hygienists and delegates from more than 40 countries will attend; plans are under way to provide facilities, translation services, and accommodation for them. All previous congresses have been held in Europe, beginning with the first in Milan in 1906. Further information is available from Dr. Leo Wade, Medical Director, Esso Standard Oil Company, 15 West 51st Street, New York, N.Y.

AMERICAN PSYCHIATRIC ASSOCIATION

On September 1, Dr. Mathew Ross, psychiatrist, formerly of Beverly Hills, California, replaced Dr. Daniel Blain as Medical Director of the American Psychiatric Association with headquarters in Washington, D.C.

CANADIAN INSTITUTE OF PHARMACY

A national pharmaceutical centre, to be known as the Canadian Institute of Pharmacy and to be located in Toronto, is the goal of a two-month fund-raising campaign being undertaken under the auspices of the Canadian Pharmaceutical Association. The centre, which will cost $300,000, will contain conference rooms, a museum of pharmacy, a library of pharmaceutical research, and office space for the Canadian Pharmaceutical Association and other organizations. The fund-raising campaign is being conducted from the headquarters of the Canadian Pharmaceutical Association, 221 Victoria St., Toronto 1.

NEW ENGLAND POST-GRADUATE ASSEMBLY

The 16th Annual New England Postgraduate Assembly, a three-day program of postgraduate medical courses for practising physicians, will be held at the Statler Hilton in Boston, Mass., November 4-6, under the auspices of the six New England state medical societies and chapters of the American Academy of General Practice. In addition to morning clinics at Boston hospitals, the program will include lectures, panel discussions, clinico-pathological conferences, luncheon symposia, medical films and scientific and technical exhibits.

A special program for wives of attending physicians has been arranged.

Further information can be obtained from: Dr. Kenneth W. Warren, Chairman, Program Committee, New England Postgraduate Assembly, 22 The Fenway, Boston 15, Mass.

INTERNATIONAL COLLEGE OF SURGEONS: MID-ATLANTIC REGIONAL MEETING

The United States Section, International College of Surgeons, will hold its Mid-Atlantic Regional Meeting at the Homestead, Hot Springs, Va., November 17-18. The scientific program will consist of 10 papers, two panels and a sound movie in colour. A banquet will be given on the evening of the first

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day. Further information from: Dr. E. G. Gill, 711 Jefferson Street South, Roanoke 13, Va.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The Part I Examinations of the American Board of Obstetrics and Gynecology are to be held in various parts of the United States and Canada on Friday, January 16, 1959, at 2.00 p.m.

Candidates notified of their eligibility to participate in Part I must submit their case abstracts within 30 days of notification of eligibility. No candidate may take the written examination unless the case abstracts have been received in the office of the Secretary.

Current bulletins outlining present requirements may be obtained by writing to the Secretary: Robert L. Faulkner, M.D., American Board of Obstetrics and Gynecology, 2105 Adelbert Road, Cleveland 6, Ohio.

RADIO STRONTIUM IN CANADIAN MILK

The Department of National Health and Welfare has established a radiochemical laboratory at Ottawa, which is engaged in making determinations of radioactive strontium content of biological samples obtained from various parts of Canada. It has now issued a preliminary report on the measurements of radioactive strontium in Canadian milk powder samples, which shows that, as in the United Kingdom and the United States, the content has manifested a pronounced upward trend in the last ten years. However, results are so variable that the authors of the report point out that it is not possible to draw firm conclusions from the data at this time.

They also mention the difficulty of estimating the radioactive strontium content of bone from estimates of its content of milk. They hope at some future time to be able to correlate bone measurements with milk determinations, and thus to arrive at a figure for the average radio strontium content of bone in the Canadian population.

NATIONAL CANCER INSTITUTE OF CANADA RESEARCH FELLOWSHIPS

The National Cancer Institute of Canada offers a number of Research Fellowships, designed to provide advanced training and experience in cancer research for those who plan a career in which furthering knowledge about cancer will be a major interest.

Fellowships are open on equal terms to men and women and are awarded to the applicants who are deemed best qualified on the evidence submitted. Candidates must be a graduate of a university approved by the Institute. Research Fellowships are normally tenable in Canada. The value of the fellowships will depend on the training and experience of the candidate. Tenure and payment of a Fellowship commences on April 1 or July 1.

Application for a Fellowship must be made by the candidate to the National Cancer Institute of Canada on an official form on or before December 15 of the preceding year.

A copy of the regulations concerning these Fellowships together with application forms may be obtained from the National Cancer Institute of Canada, 800 Bay Street, Toronto 5, Ontario.

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B.M.A. CLINICAL PRIZES

The British Medical Association draws the attention of its members once more to the competition for the Sir Charles Hastings and Charles Oliver Hawthorne Clinical Prizes, awarded for the best and second best entries respectively in a competition established to promote systematic observation, research and record in general practice. Essays submitted must include personal observations and experiences collected by the candidate in general practice. Any member of the British Medical Association is eligible to compete. Entries must be sent to the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1, not later than December 31, 1958.

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THE WORK OF WHO*

The Annual Report for 1957 of the Director-General of the World Health Organization particularly stresses the coordination of research, both in the laboratory and in the field. It contains many illustrations of work undertaken on these lines and in relation to various infectious diseases as well as to resistance to insecticides, the great problem in malaria control. It describes the way in which WHO is helping governments in 76 countries to eradicate malaria.

There is naturally a full description of the 1957 influenza epidemic and the way in which the worldwide epidemiological system assisted in providing information on the spread of the disease and on the type of virus to which it was due. Work on vaccines includes the elaboration of a highly stable dried smallpox vaccine.

The special training required by medical and public health workers to meet the problems arising from the increased use of atomic energy in medicine and industry is discussed.

All the many other aspects of the work of WHO find a mention in this report.

*The Work of WHO 1957. Annual Report of the Director-General to the World Health Assembly and to the United Nations. Official Records of the WHO No. 82. 183 pp. World Health Organization, Palais des Nations, Geneva. $1.25.

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THE AMERICAN COLLEGE OF CHEST PHYSICIANS

The American College of Chest Physicians has produced a very full and detailed directory of its members in the form of a Silver Anniversary Edition 1959. This membership roster contains not only biographical details of members but also the statement of objectives of the organization, its bylaws, its governing bodies and its awards. It is obtainable from the American

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College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

TROPHIC ULCERS

Trophic ulcers occurring as a complication of Raynaud's phenomenon are painful and often resistant to treatment. Sherbel and associates (*Cleveland Clin. Quart.*, 25: 92, 1958) used 2 to 5% iproniazid (Marsilid phosphate) ointment in a water-soluble base in the treatment of 23 patients. This group consisted of 14 patients with progressive systemic sclerosis, five patients with acrosclerosis complicated by ulceration of the fingertips and two patients with advanced Raynaud's disease. Of the group, 19 had complete relief of pain and 18 had complete healing of the ulcers. However, in eight patients the pain and ulcers recurred within three weeks to six months after temporary discontinuance of the treatment.

RADIATION FROM FUTURE FALL-OUT FROM WEAPON TESTING

Consideration is given by Inglis (*Science*, 127: 1222, 1958) to the radiation dosage which will be met on earth in the coming years in any of the three following eventualities: if nuclear weapon testing continues at its present rate, or if testing ceases now, or if the rate of testing continues to increase at the average rate at which it has increased since 1951. These computations are based mostly on the fall-out of Sr^{90} of which there is supposed to be 0.5 mc/mi^2/megaton distributed over the earth's surface in any blast that reaches the stratosphere. It is estimated that approximately 30 megatons' equivalent of fission products had been liberated by the end of 1956.

If testing had been stopped at the end of 1956, the maximum intensity of ground radiation from Sr^{90} would be reached in 1970 and would represent approximately 2.75 times that at the end of 1956. After that date it would slowly decrease through disintegration over the years. If the tests should continue at a steady average rate, the ground intensity would rise to approximately 32.5 times as much as it was at the end of 1956. Should the rate of testing keep on increasing as it has since it was started the ground intensity in 100 years would be about 730 times as great as it was at the end of 1956.

Large as these figures may seem, their full significance is not obtained unless they are compared to other values more commonly known. For this purpose the author draws a very interesting comparison. It appears that residents of the western suburbs of Chicago, who drink deep well water containing about ten times as much radium as average drinking water, have an internal dose due to radium greater than the dose they would have from strontium if the surface density of Sr^{90} were 3000 mc/mi^2. The author hastens to add that "even with our most pessimistic assumption of a steadily increasing rate of testing, it would

take about 125 years for the world wide average density of Sr^{90} to reach this level".

His conclusions are to the effect that "judgment should not be unduly swayed by one prediction of human suffering if the alternative were to increase appreciably the likelihood of a much greater catastrophe".

LACK OF SCIENTIFIC VALIDITY OF BODY SURFACE AS BASIS FOR PARENTERAL FLUID DOSAGE

A review of the literature regarding measurement of body surface area and its relationship to basal metabolism leads Oliver and co-workers (*J. A. M. A.*, 167: 1211, 1958) to the conclusion that this procedure lacks the accuracy which is usually ascribed to it. They reject this method as being unnecessarily complicated and no more accurate than a simple rule of thumb based on weight alone for the purpose of estimating the metabolic needs of infants and children. This rule is adjusted to age as well as to weight, and tables given show the amount of fluid required for maintenance. It varies from 60 ml./lb. of body weight in infants under one year of age to 35 ml./lb. in children aged 11-14. Correction of dehydration is started with 90 ml./lb. per 24 hours and is adjusted using not only body weight but clinical judgment as well.

ABSTRACTS ON GERONTOLOGY

The Excerpta Medica Foundation has launched the twentieth section of its abstracting service—a section dealing with articles on gerontology and geriatrics. Publication will appear monthly as from July 1958 and each yearly volume will contain approximately 700 pages. The subscription fee is $15 per annum. *Gerontology and Geriatrics* has begun publication in cooperation with the U.S. National Heart Institute and National Institute of Mental Health, and with the aid of a grant from the U.S. Public Health Service. It aims to cover the whole field of aging and the aging process, and to be of value not only to physicians but also to social scientists.

REDUCING THE RADIATION HAZARD ASSOCIATED WITH PHOTOFLUOROGRAPHY

To test the effectiveness of devices designed to reduce radiation hazards associated with photofluorography, a masonite phantom was constructed by Goldman and Shultz (*Am. Rev. Tuberc.*, 77: 923, 1958), which had approximately the same density as human tissue. Radiation exposure to gonads and skin was estimated with appropriately placed dosimeters. Several hundred exposures were made to test the effect of: (1) a lead diaphragm at the tube port to confine the primary beam to the desired area; (2) local shielding of the lower half of the examinee's body

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by leaded rubber; and (3) additional filtration of the x-ray beam. Use of these three simple devices reduced radiation received by the gonads tenfold, and the skin dose by 50%. Since the irradiation associated with photofluorography is considerably greater than that from conventional roentgenography of the chest, it is mandatory that photofluorographic x-ray installations be properly shielded (as has been done in Canada).

COMMUNITY TRIALS OF BCG VACCINATION

After a follow-up period of six to seven years of two controlled trials of BCG vaccination, initiated and directed by the U.S. Public Health Service, Palmer and his colleagues have issued a progress report (*Am. Rev. Tuberc.*, 77: 877, 1958). One trial, on children aged one to 18 years, was in Puerto Rico; the other, on persons more than five years of age, was in three counties in Alabama, where the tuberculosis problem is similar to that in many other communities in the U.S.A. More than a quarter of a million persons were placed under study: 112,000 tuberculin reactors, and 144,000 nonreactors who were allocated by a randomization scheme to vaccinated and control (unvaccinated) groups. For the identification of new cases of tuberculosis appearing in the study populations, the established medical, public health, and vital statistics reporting systems were deliberately chosen as being sufficient for the purpose of the study.

The most striking finding of both trials was that the risk of developing tuberculosis was much greater for persons who were tuberculin reactors on entry than for those who were nonreactors. Of the total number of cases that appeared during the follow-up period, 75% were among reactors; consequently, only the 25% of the cases that would have appeared among the initial nonreactors could have been prevented if vaccination had been completely effective.

Tuberculosis case rates among nonreactors were low. In Puerto Rico the rate was 43 per 100,000 per year among controls and 30 among vaccinees. The difference, representing 31% fewer cases among the vaccinees than among the controls, is statistically significant. In the Alabama trial, the corresponding rates were 22 among controls and 14 among vaccinees, but the difference (36%) is not statistically significant.

The authors feel that the low case rates among nonreactors can be directly attributed to the present low risk of acquiring new infections. Because BCG cannot help those who are already infected, or those who will not become infected in the future, it is considered that vaccination cannot be very useful in controlling tuberculosis in the U.S.A. Moreover, with the rapid decline in tuberculous infection, the tuberculin test is considered to be increasingly more valuable for epidemiologic, case-finding and diagnostic purposes. These uses of the tuberculin test are, of course, destroyed by

vaccination, which makes it virtually impossible to identify the naturally infected persons. The position is taken by the writers that in most situations in the U.S.A. today the advantages of vaccination are outweighed by the disadvantages.

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PRIMARY HYPERTENSION AND HYPERTENSIVE DISEASE IN EARLY CHILDHOOD

Within five years, 11 hypertensive children under 10 years of age were seen by Borhani and Lee (*Am. Heart J.*, 55: 796, 1958). Four of these cases are considered true cases of primary hypertension. It is emphasized that the vast majority of such cases are due to or found in connection with renal disease, particularly chronic pyelonephritis. In spite of its being rare, essential hypertension does occur in children, and routine checking of blood pressure in patients of all ages is therefore necessary.

THE BACTERIAL RESISTANCE PROBLEM

A world-wide picture of the clinical problem of bacterial resistance and methods of dealing with it will be presented at the International Colloquium on Resistant Infections at the Plaza Hotel, New York City, on November 20 and 21. The conference is being sponsored jointly by the United States Committee, World Medical Association, and Eaton Laboratories, Norwich, N.Y. Physicians from Argentina, Canada, England, France, Germany, Puerto Rico, Sweden and the United States will describe the results of their investigations and their experiences in treating resistant infections.

Particular emphasis will be placed on the control of staphylococcal infections in hospitals. The role of drugs, both as contributors to the development of resistance and as a means of helping to solve the problem, and the need for more rigid aseptic techniques to control the spread of infectious organisms, will be thoroughly discussed.

All the medical disciplines concerned with the resistance problem will be covered in conference sections dealing with systemic, respiratory, topical and urinary tract infections. A final session will be devoted to the role of the hospital environment in disseminating infection.

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WORLD-WIDE ABSTRACTS

This October, a new abstracting journal for general practitioners made its appearance. *World-Wide Abstracts of General Medicine* is published by the Excerpta Medica Foundation and distributed as a service to physicians by Warner-Chilcott Laboratories. It will appear monthly and contain selected abstracts designed to provide the general practitioner with news of particular significance in his work. In addition to abstracts each issue will contain a review article. In the first issue, for example, Paul Dudley White discusses the management of coronary thrombosis.